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## EDITORIAL

# Role of journal clubs in undergraduate medical education in India

**Mahanta Putul\***

A journal club is a group of people who meet regularly to critically evaluate recent articles in the academic literature, such as the literatures in the medical field and other scientific areas. It helps in simplifying the application of evidence-based medicine to some other areas of medical practice. Participants in journal club can express their views about the appropriateness on the research questions, hypothesis, design and statistical analysis of the article discussed.

Clinical research gives us the insight to learn to prevent, diagnose, and treat illnesses, hence directly impacting people's health. It involves different elements of scientific investigation and human participation. Training in clinical research,<sup>1</sup> therefore, highlights the extent of needs for research-oriented medical education throughout the country which is an important need at the present juncture. There is a need to involve the undergraduate medical students in rigorous research activities at the medical colleges and universities to improve the research-oriented medical education where journal club may play an active role.

### THE CURRENT SCENARIO IN INDIA

India has a history of scientific research and publications. Big debates are going on among the scientists, researchers and educators in the field of scientific research and publication. Considering the population growth, publications and patent production in India were marginally low as compare to other developing and developed country.<sup>2</sup> Irrespective of research subjects, a total of 157 researchers per million populations were reported in India in the year 2010, much less than the global average of 1023.<sup>3</sup> As far as research in medical sciences is concerned, India raised with 12<sup>th</sup> position among the productive countries of the world in medicine during 1999 to 2008 with a simple 1.6% share in the world research output.<sup>4</sup> In the year 2015 India ranked 5<sup>th</sup> position in the production of the publication. The USA, China, United Kingdom, and Germany are in the leading position.<sup>2</sup> But, most of these researches of India were the faculty members and scientists from reputed medical institutes, and very little had been contributed by students.<sup>5</sup> Interesting fact is that in India out of 10,000 research efforts, only 4 comes out as a successful researcher, India ranks below Kenya, Chile, Brazil, and China.

Investment in research and development in India is very poor, which is only 0.9% of its GDP, whereas China, Russia, and Brazil spend more on it than India.<sup>2</sup>

Therefore, the needs of the undergraduate biomedical research (BMR) in India is to be reinforced with all keenness, at the time while the BMRs of faculties are striving stiff to get momentum among the medical colleges in India. It is a fact that cost implications often become the limiting factor in exposing undergraduate students to large scale clinical trials in resource-limited scenario besides other facilities. Therefore, we need some alternative approaches to stimulate critical appraisal skills among medical students who are going to be a future researcher.

### EVOLUTION OF SCIENTIFIC PUBLISHING: KEY DATES<sup>6</sup>

KEY YEARS	EVOLUTION OF SCIENTIFIC PUBLISHING
1323	Compagnie du Gai Sçavoir, the oldest learned academy on record was founded in Toulouse, France.
1660	The Royal Society of London was founded for the improvement of natural knowledge.
1665	First scientific journal was published, i.e., Journal des Scavans and Philosophical Transactions of the Royal Society of London. The journal used some form of peer review system, although not exactly like today's version.
1731	Medical Essays and Observations, the first fully peer-reviewed journal was launched by the Royal Society of Edinburgh.
1743	The American Philosophical Society, the first scholarly society in what is now the US, is created.
1820	First specialist journal was published.
1848	The American Association for the Advancement of Science (AAAS) was founded. AAAS publishes the journal Science and is the largest general scientific society in the world.
1869	Nature publishes its first issue.

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Key years	Evolution of scientific publishing
1870	References began to be collected at the end of the articles.
1880	Science publishes its first issue.
1920	First summaries appeared at the end of the article.
1930	First paper on the use of statistics was published.
1947	Elsevier, the longtime publishing giant, launches its first international journal, <i>Biochimica et Biophysica Acta</i> .
1950	Widespread use of IMRAD format.
1960	Summaries began to be collected at the end as an abstract.
1970	Database was introduced.
1980	First international conference on peer-review was organized.
1990	Introduction of electronic journal was initiated. Postmodern Culture becomes the first online journal.
1991	arXiv, the science pre-print server was launched.
2003	The Public Library of Science (PLOS) was founded.
2006	PLOS ONE, the wildly successful open access megajournal, begins publishing.
2013	PLOS ONE publishes 31,500 articles.
2010	The altmetrics manifesto, describing potential new ways to gauge the impact of research beyond citations and impact factors was written.
2012	Several innovative and relatively new journals, including F1000 Research, Peer J, and eLife, are launched. These journals are experimenting with new forms of peer review, new business models and new funding sources.

The above data shows how the scientific society was formed with the defined objectives for promoting cooperation among scientists in different fields, defending scientific freedom, encouraging scientific responsibility, supporting scientific education and science to outreach for the betterment of the society.

Journal club is one of such tools that can enrich the scientific literature and help in improving medical education in the era of evidence based medicine. The credit for the establishment of the first formal medical journal club goes to William Osler, who founded the journal club at the McGill University in North America in 1875.<sup>7</sup>

### ROLE OF JOURNAL CLUB

A journal club among undergraduate students will help them to develop and to increase the inquisitiveness about scientific reading. Picking up an article for discussion will surely build the critical thinking capacity in the young minds. This will increase their competency in application of theoretical principle

and basic doctrine of research. Once they are acquainted with the process of reading scientific articles, they will develop the curiosity about novelty on the subjects which ultimately will build a group of future researchers. Medical science is an evolving entity and our clinical practice should corner around Evidence Based Medicine.

‘Evidence-based Health Care (EBHC)’ could best be integrated with medical student training to enhance student’s knowledge, attitude, and skills regarding EBHC. In the era of evidence based medicine, analyzing the quality, validity, and relevance of the evidence should be a skill that must be taught from undergraduate level<sup>7</sup> to improve the standard of medical education in India and journal club can be used for this objective.

Understanding the reading habits of medical students of scientific journal provide insights and opportunities for medical educators to evaluate the learning needs of the students and improve the teaching methods. Many of us read scientific journal for some specific reason.

Some of the common reasons why people read a scientific journal are as follows:

- To impress
- To learn clinical features and causes
- To distinguish useful from harmful
- To keep abreast of professional news
- Whether to use a new or existing diagnostic test, etc.

Medical literature is continuously mounting in all of its areas. The concepts, ideas, and beliefs in different fields are undergoing a rapid revolution. Therefore, academicians, researchers, practitioners, and students to keep updated knowledge on the subject. So, the benefits of a journal club can be used to remain current with the medical literature which offers an opportunity to learn methods of critically evaluating journal articles. It can be organized around a defined subject in basic or applied research.

The activities of a journal club are commonly seen in postgraduate medical education in India; however, it is relatively underused in undergraduate medical education. It can be a very effective platform where the students can gather first-hand knowledge on analyzing, evaluating, dissecting, and utilizing the scientific literature.

Journal clubs and letter writing exercises are innovative ways of teaching critical appraisal to medical undergraduates, and the response from the students have also been positive.<sup>8, 9</sup> It motivates reading behaviors of physicians-in-training and also increase knowledge of epidemiology and biostatistics.<sup>10</sup> Undergraduates can plan, structure sessions with well-defined learning objectives, suitably designed to evoke participants<sup>2</sup> interest and attendance which are essential to the functioning of a journal club.<sup>11</sup>

The evaluation of the journal clubs can be done through periodic internal assessment and evaluation tests. The number of correspondences through letters to the editor, getting

accepted for publication, based on the specific questions remaining unanswered regarding the original articles discussed may also be an indicator of the efficacy of the club.<sup>12</sup>

Subsequent discussions of journal club on receipt of reply from the editor or author to a published letter to the editor or article in a subsequent session, enhances the insight on the topic further.

Epidemiology and biostatistics are generally taught under the Community Medicine subject during the period of 3<sup>rd</sup> professional MBBS Part-1 to Indian Medical Graduates. As the knowledge of biostatistics is essential in biomedical research and publications and since by the time a student enters 3<sup>rd</sup> professional tenure they possess appreciable knowledge on biostatistics, journal clubs can be introduced at this stage onward which will be more meaningful<sup>7</sup> and effective.

The quality of a research paper can be measured by their citation index. Currently, India is lagging behind in citation index as compared to other leading countries.<sup>2</sup> A journal club helps in doing quality research and its subsequent publication.

Many of us may be arguing about the feasibility of conducting journal clubs for huge batches of undergraduates, but the problems may be overcome by using the tutorial or discussion classes in smaller batches.

## CONCLUSION

Making journal clubs part of the medical curriculum may thus benefit the purpose of exposure of students to the world of frontline research, and pave their way for a future entry in the world of translational research.

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**Address for correspondence:**

\*Editor-in-chief

Int J Health Re Medico Leg Prac

Professor and Head, Forensic Medicine and Toxicology

Assam Medical College, Dibrugarh, Assam

**Email:** drpmahanta@gmail.com

**Mobile:** +919435017802



## ORIGINAL RESEARCH PAPER

# A clinico-bacteriological study of leprosy cases in a tertiary care hospital of North-East India

Borah AK<sup>1</sup>, Bora Simi<sup>2</sup>, Kataki Monjuri<sup>3</sup>, Hussain Ezaz<sup>4</sup>

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## ABSTRACT

**Introduction:** Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. Although the elimination target has been achieved at the national level, leprosy still continues to be an important disease in several parts of India. Slit-skin smear microscopy plays an important role in an early and accurate diagnosis. **Materials and methods:** All clinically suspected referred cases of leprosy from dermatology department during the time period were included in the study. After taking detailed history and physical examination, Slit Skin Smears were done in all cases. All the slit skin smear were examined by doing Z-N staining and cases were classified as multibacillary or paucibacillary on the basis of result of smear examination. **Result:** Out of 144 cases, 72.22% (104/144) were male and 27.78% (40/144) were female. Age of the patients ranged from 7 years to 72 years. Majority of cases 48.61% (70/144) were of age group 20-39. Majority of the patients (121/144, 84.03%) were from lower socio-economic background where as 15.97% (23/144) patients were from middle income group. Hypopigmented patch (63.89%, 92/144) and nodular lesions (59.72%, 86/144) were common presentations and few cases with loss of extremities along with ulcer. Out of 144 cases, 36 cases (25%) showed smear positive and 108 cases (75%) showed smear negative on slit skin smear examination. **Conclusion:** So many years after the study, leprosy still remain as important problem to bring it under expected level of control. This study indicates high circulation of lepra bacilli in the community in the "elimination era". There is an urgent need for early diagnosis and appropriate treatment to prevent spread of the bacilli and development of disabilities.

**Keywords:** Hypopigmented; Acid fast; Multibacillary; Slit skin smear; Paucibacillary; Nodular.

## INTRODUCTION

Leprosy (Hansen's disease) is a chronic granulomatous disease caused by a bacillus, *Mycobacterium leprae*, mainly affecting the peripheral nerves, skin, mucosa of the upper respiratory tract and eyes. It is an infectious disease transmitted by droplets from the nose and mouth of untreated cases.<sup>1</sup>

Leprosy is one of the oldest known human diseases associated with serious physical and functional disabilities. Due to the case load and social stigma attached to the disease, leprosy still continues as a disease of public health concern.<sup>2</sup> According to WHO report (updated on October 2017), 1,76,176 cases of leprosy were prevalent (0.18 cases per 10,000 people) at the end of 2015 and 2,11,973 people developed leprosy (0.21 new cases per 10,000 people) during the year globally. According to this report, 2,13,899 and 2,15,656 number of new cases was reported in the year 2014 and 2013 respectively indicating the degree of continued transmission of infection.<sup>1</sup>

Pockets of high endemicity still remain in some areas of many countries including India. India alone accounted for 58.85%<sup>3,4</sup> of the global leprosy burden and a total of 1,27,000 new cases were detected during 2013-14. A total of 86,000 cases

## Address for correspondence:

<sup>1</sup>Assistant Professor

**Email:** borahamrit6@gmail.com

**Mobile:** +917002953295

<sup>2</sup>PGT (Corresponding author)

**Email:** simibora10@gmail.com

**Mobile:** +918822737765

<sup>3</sup>Associate professor, <sup>4</sup>Statistician

Dept. of Microbiology

Assam Medical College and Hospital, Dibrugarh, Assam.

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were recorded on April 1, 2014 (prevalence rate of 0.68 per 10,000 population).<sup>4,5</sup>

India is one of the highest disease burden country due to leprosy. The current scenario reflect high circulation of lepra bacilli in the community. Prompt early detection of cases and appropriate treatment is required to prevent the spread of bacilli and development of disabilities.<sup>5</sup>

The three cardinal signs for confirmation of diagnosis of leprosy include hypo-pigmented or reddish skin lesion with definite sensory deficit, involvement of the peripheral nerves, demonstration of *M. leprae* in the lesions.<sup>6</sup> Leprosy is most commonly diagnosed by clinical signs and symptoms.<sup>7</sup> Demonstrations of *M. leprae* in the lesions by examination of the slit skin smear confirm the diagnosis. Bacteriological identification by slit skin smears examination plays an important role in early and accurate diagnosis of leprosy. In some multibacillary cases with infiltrative lesions of the skin without loss of sensation especially during early stages, positive skin smear may be the only conclusive sign for diagnosis of the disease.<sup>6</sup> With these concern, the present study aims at describing the epidemiological and clinico-bacteriological pattern of leprosy patients depending upon bacterial load based on "Slit skin smear" technique among the patients mainly from upper Assam area in order to help strengthen control activities in the "post elimination era."

## MATERIALS AND METHODS

This was a prospective, observational study. The study was

conducted at the department of Microbiology, Assam Medical College and Hospital (AMCH) during a period of one year from October 2016 to September 2017. All clinically suspected referred cases of leprosy from dermatology department during the time period were included in the study.

Informed consent was taken from all patients enrolled in the study and data was recorded. In each case, detailed history was taken and physical examination was done. Demographic data and clinical details were recorded with particular reference to the symptoms, duration, initial site of appearance of lesion, extension of lesions, distribution and colour of lesions, presence of nerve involvement in the form of thickening or tenderness, presence of disability, history of contact with leprosy cases, family history of leprosy, socioeconomic background.

Slit Skin Smears were done in all cases. Skin smears were collected from 4 sites including both the ear lobules, and margins of active lesions and nasal swab specimens. The air-dried and heat fixed smear were stained with Zeihl Nelson stain and cases were classified as multibacillary or paucibacillary on the basis of result of smear examination.<sup>8</sup>

Statistical analysis was carried out using Microsoft Office Excel 2007 software. Data was analyzed for descriptive statistical analysis using percentage & proportion.

## RESULTS

Total 144 clinically diagnosed cases were included in the study during the period of one year.

**Table 1** Distributions of cases according to socio-economic characters

Socio-demographic factors		Frequency (n=144)	Percentage (%)
Age (years)	0-9	4	2.78
	10-19	27	18.75
	20-29	32	22.22
	30-39	38	26.39
	40-49	22	15.28
	50-59	14	9.72
	60-69	6	4.17
	70-79	1	0.69
Gender	Male	104	72.22
	Female	40	27.78
Residence	Rural	118	81.94
	Urban	26	18.06
Socioeconomic group	Lower group	121	84.03
	Middle group	23	15.97
	Higher group	0	0
Family history/history of contact	Yes	18	12.50
	No	126	87.5
Occupation	Tea garden worker	48	33.33
	Agriculture labour	34	23.61
	Others	62	43.06



### Demographic characteristics:

Age of the patients ranged from 7 years to 72 years. Maximum patients 48.61% (70/144) (**Table 1**) belonged to age group 20-39 years and 8.33% (12/144) of total patients were children. The percentage of cases in infants were nil.

Gender wise male patients (72.22%, 104/144) were more common than females (27.78%, 40/144). Male to female ratio (M:F) was 2.6:1.

Most of the cases in this study were without past history of exposure, only few had intra-familial contact history (18/144, 12.50%). 81.94% of cases were from rural area and 18.06% from urban area.

Majority of the patients (121/144, 84.03%) were from lower socio-economic background where as 15.97% (23/144) patients were from middle income group. There were no patients from high income group.

Maximum number of patients 48(33.33%) were found to be tea garden worker. The next common was agriculture labour 34(23.61%).

### Clinical pattern:

Maximum number of patients 73(50.69%) (**Table 2**) in this study had the duration of illness less than 6 months, between 1-5 yrs in 39 cases (27.08%) and 6-12 months in 32 cases (22.22%).

Hypopigmented patch was the commonest presentation (63.89%, 92/144), extremities (119 cases, 82.64%) were the most common sites involved followed by nodular lesions (59.72%, 86/144), loss of sensation (53.47%, 77/144), thickened nerves (35.42%, 51/144), erythematous patches (34.02%, 49/144), trophic ulcers (17.36%, 25/144), limb deformities (3.47%, 5/144), loss of extremities (2.78%, 4/144).

Among the patients presenting with hypopigmented patches, majority of the patients (64/92, 70.65%) had patches ranging between 2 to 5, 12(13.04%) patients had patches 6 or more than 6 and 16 patients (17.39%) had single patch. Patches were located mainly on uncovered part of body or the part of body which can be easily discovered by patient such as face, hands. Only 21(22.83%) patients had patches on covered area or the area which is not accessible to be seen by patient; whereas 71 patients (77.17%) had at least one or some patches on the uncovered body part or the area which can be seen by patient easily.

Nerve involvement was seen in 35.42% patients. Multiple nerve involvement was present in 27(18.75%) patients. Ulnar nerve (23, 45.09%) was the most commonly affected nerve. Non healing ulcer on extremities was seen in 25(17.36%) patients.

5(3.47%) cases had bony deformity in the form of claw hand. No cases of foot drop were observed. 2(1.38%) patients presented with nasal flattening. There was no case observed as ocular manifestation. 4 cases (2.78%, 4/144) presented with loss of extremities or limb amputation.

### Bacteriological findings:

On examination of Slit skin smears after AFB staining, 36 cases (25%) (**Table 3**) showed smear positive (multibacillary) and 108 cases (75%) showed smear negative (paucibacillary).

**Table 2** Distribution of cases according to duration of illness

Duration	Frequency (n=144)	Percentage (%)
<6 months	73	50.69
6-12 months	32	22.22
>1 year	39	27.08

**Table 3** Classification of cases according to Slit skin smear results

Classification	Frequency (n=144)	Percentage (%)
Paucibacillary	108	75
Multibacillary	36	25

### DISCUSSION

Leprosy can occur at all ages ranging from early infancy to very old age.<sup>9</sup> In the present study, majority of patients (70; 48.61%) belonged to the age group of 20-39 years which represents the reproductive active age group in both sexes. According to this study, patients below 7 years were affected the least.

Similar observations were made by Guha et al.,<sup>10</sup> Kaur et al.,<sup>11</sup> Sehgal et al.,<sup>12</sup> Moorthy et al.,<sup>13</sup> Kaur et al.,<sup>14</sup> Thakkar et al.,<sup>15</sup> Swarnakumari et al.,<sup>16</sup> Premalatha et al.,<sup>17</sup> Pokhrel et al.<sup>18</sup> Thus, the age distribution observed in present study correlates well with that of the other previous studies.

The frequency of leprosy cases in children is an indicator of the level of transmission of the disease in the community. In the 7-19 years of age group, there were a total of 31 cases and 8.33% (12/144) of total cases were children (7-12 years). This indicates a high infectivity status in the community.

Leprosy affects both sexes. But, in most parts of the world, males are affected more frequently than females often in the ratio of 2:1.<sup>9</sup> The present study also showed concurrence with the ratio of 2.6:1 indicating the same. This was also observed in the studies by Sehgal et al.<sup>12</sup> and Moorthy et al.<sup>13</sup> Male predominance may be due to factors like industrialization, urbanization, more opportunities for contact in males, difference in health seeking behaviour of males and females who are often slow to self report.

In the present study, 84.3% of the patients were from low income group and 15.97% were from middle income group. This results correlates with some other previous studies. Similar observations were made by Swarnakumari et al.<sup>16</sup> where 80% of the patients were from low income group. Sing et al.<sup>19</sup> found that 57.1% of the respondents belonged to poor socio-economic status followed by 21.6% in lower-middle class group. Major percentage of cases in lower

income group may be due to factors like poor living conditions, overcrowding, poor sanitation, poor nutrition, lack of personal hygiene and illiteracy.

It has been documented that the risk of developing leprosy is nine times higher in household of patients and four times higher in direct neighboring houses of patients compared to households that had had no such contact with patients.<sup>20</sup> The present study showed that only a small proportion of leprosy cases (12.50%) had history of contact with leprosy patients. This is a positive sign. Similar observations were also made by Thakkar et al.<sup>15</sup> and Swarnakumari et al.<sup>16</sup>

The present study showed majority of patients from rural area (81.94%) which may be due to factors like lack of awareness, low accessibility to health care facilities, lack of adherence to therapy, lack of knowledge regarding the consequences of the disease and inhibition of reporting for treatment due to the social taboos and customs. Kadam et al also found that major percentage of cases belonged to rural area.<sup>21</sup>

In the present study, the duration of the illness by the time of presentation were less than 6 months in 50.69%, 6-11 months in 22.22% and 1-5 yrs in 27.08% of cases. Similar observation was also made by Swarnakumari et al.<sup>16</sup> Majority of patients (50.69% of cases) reported relatively early i.e. within 6 months of disease. But the percentage of early reporting must be further increased to prevent disease complications. Due to factors like lack of knowledge, ignorance, social taboo and customs, patients tend to hide their disease and delay their treatment at the time when they could have been easily cured.

In the present study, the disease was most common among the tea garden workers (33.33%). Agriculture labour (23.61%) was the next common occupational group. Factors like illiteracy, ignorance, lack of knowledge about the consequences of the disease, overcrowding, poor personal hygiene, malnutrition which are associated with low economic status are also more common among people pursuing the manual labour work.

In the present study, hypopigmented patches (63.89%) were the most common clinical presentation followed by nodular lesions (59.72%). Extremities (82.64%) were the most common site involved. These results correlates well with other similar studies. Kadam et al<sup>21</sup> also observed that 76.19% cases were presented with patches. Grover et al<sup>22</sup> found that upper extremity (29% cases) was the most common site involved followed by lower extremity (23% cases).

In this study, 17.36% cases showed trophic ulcers, 3.47% cases had bony deformity in the form of claw hand, 1.38% cases presented with nasal flattening and 2.78% with loss of extremities or limb amputation. These results suggest delay in diagnosis and treatment and lack of disease awareness in the patients.

In our study, 36 cases (25%) showed smear positive (multibacillary) and 108 cases (75%) showed smear negative (paucibacillary). Another study by Kakkad et al<sup>23</sup> observed

that majority (thirty-five) of the cases were AFB positive (multibacillary) and fifteen were AFB negative (paucibacillary) out of 50 cases. A study on childhood leprosy by Vukkadala et al<sup>24</sup> found that 73.17% of cases belonged to paucibacillary and 26.83% cases to multibacillary.

**Limitations:** Patient attending the out-patient and in-patient department of Dermatology, Assam Medical College and Hospitals, Dibrugarh. Patients were mainly from upper-Assam area. Hence, there is limited information about the epidemiology of the disease. The study duration was only one year. So, further studies with longer duration are required to know the disease status better.

For diagnosis of leprosy, there is no independent gold standard method. Taking any of the clinical signs and symptoms, slit skin smear results, histopathological parameters as a gold standard is not ideal. Variation of results in different studies may be due to different criteria used to select the cases. Various factors also influence the results such as differences in sample size, age of the lesion, immunological and treatment status of the patient at the time of taking smears for SSS examinations.

## CONCLUSIONS

Leprosy still remain as important problem to bring it under expected level of control. This study indicates high circulation of lepra bacilli in the community in the “elimination era”. There is an urgent need for early diagnosis and appropriate treatment to prevent spread of the bacilli and development of disabilities. Awareness programmes should be designed to motivate the community for self-examination and reporting.

**Conflict of Interest:** None.

**Ethical clearance:** Taken.

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**Authors Contribution:** We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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## ORIGINAL PAPER

# Seroprevalence of dengue cases in a tertiary care hospital

Raja Dina<sup>1</sup>, Sarma Vaishali<sup>2</sup>, Das Parasmitta<sup>3</sup>, Goldar Shalini<sup>4</sup>, Phukan Chimanjita<sup>5</sup>

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## ABSTRACT

**Background:** Dengue is a mosquito borne viral disease of global public health concern and is a major cause of morbidity in most of the endemic regions of the world. In northeast India, particularly Guwahati, Assam has been experiencing dengue every year with high morbidity since its first outbreak in 2010 and therefore emerging as major public health concern in northeast India and spreading with increased morbidity.

**Objective:** To analyse the seroprevalence and epidemiological trend of dengue among patients presenting in Gauhati Medical College and Hospital from the year 2012 to 2017. **Materials and methods:** A retrospective study was done from the year 2012 to 2017 in blood samples received in the department of Microbiology, Gauhati Medical College & Hospital. Dengue NS1 antigen and Dengue IgM antibody ELISA tests were performed for the confirmation of dengue cases which was performed as per the manufacturer's guidelines. We estimated the incidence by applying age and sex distribution of Dengue cases in Assam. **Results:** From the six years study we found that the prevalence of Dengue was highest in 2012 (47%) and lowest in 2014 (10%). Highest sample load was seen in 2016. In all the years, males patients were more than the female patients. Commonest age-group of the affected patients was between 25- 34 years of age. In Assam, Kamrup (Metro) district followed by Kamrup (Rural) showed highest case load in all the years. **Conclusion:** Dengue has remained a persistent problem in Assam with the increasing distribution range of *Aedes aegypti*. There is a need of identification of high-risk areas, vector incrimination and seasonal infectivity of dengue so that future outbreaks can be avoided by targeted interventions

**Keywords:** IgM antibody; NS1 antigen; ELISA.

## INTRODUCTION

Dengue is seen as a global epidemic with recorded prevalence in more than 120 countries.<sup>1</sup> Dengue is caused by dengue

virus (DENV) belonging to genus *Flavivirus* of family Flaviviridae that comprises four serotypes (DENV 1–4) and transmitted in humans by *Aedes* mosquito species. Infection may range from mild, self limiting febrile illness (dengue fever) to a more severe form of dengue haemorrhagic fever and dengue shock syndrome.<sup>2</sup>

In northeast India, particularly Guwahati, Assam has been experiencing dengue every year with high morbidity since its first outbreak in 2010.<sup>3</sup> Guwahati is the largest and fast-growing metropolis and gateway of northeast India. Over the past decade, there has been an increase in urbanization, deforestation, massive developmental activities, rapid population movement and increased air connectivity between Guwahati and other metropolitan cities resulting in increased receptivity for mosquito breeding and possible importation and spread of dengue virus through the human host in the region. The disease is currently spreading to semi- urban areas of other districts of Assam supported by serological evidence for circulating dengue virus serotypes.<sup>4</sup>

Dengue infection is usually confirmed by identification of viral genomic RNA, antigens, or the antibodies it elicits. Antigen detection tests based on NS1 detection have been designed to detect the dengue viral NS1 protein which gets released from the dengue infected cells and appears early in the

## Address for correspondence:

<sup>1</sup>Associate Professor

**Mobile:** +919864039629

**Email:** dinaraja2016@gmail.com

<sup>2</sup>Demonstrator

<sup>3</sup>Demonstrator, <sup>4</sup>PGT,

<sup>5</sup>Associate Professor (**Corresponding Author**)

**Mobile:** +919864093483

**Email:** chimanjitaphukan@gmail.com

Department of Microbiology

Gauhati Medical College and Hospital, Guwahati

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bloodstream. ELISA-based serological tests are easy to perform and are cost-effective for dengue detection.<sup>5</sup>

Dengue fever represents a real economic burden especially in affected countries and endemic areas including Assam. Widespread efforts are needed to reduce disease spread and lessen the mortality rates and the associated healthcare cost. There is a need for more scientific research which we believe is a key route to provide further insight into the pathogenesis of dengue infection to understand the distribution and reasons for repeated endemicity. Hence we have conducted this research and compiled relevant data so as to understand the distribution and prevalence of dengue infection in Assam.

This paper has analyzed the seroprevalence and epidemiological trend of dengue cases tested in Gauhati Medical College and Hospital from January 2012 to December 2017.

### MATERIALS AND METHODS

Blood samples were collected and processed in the Department of Microbiology, Gauhati Medical College & Hospital. This centre is one of the dengue sentinel surveillance sites in the country under the National Vector Borne Disease Control Program (NVBDCP) of India. Patients attending the various departments of GMCH and those referred from different hospitals and laboratories, with clinical suspicion

of dengue were screened over a period of six years from January 2012 to December 2017. The patients presenting with fever of sudden onset with headache, retrobulbar pain, conjunctival injection, pain in back and limbs, lymphadenopathy and maculopapular rash, haemorrhagic manifestations, who had recent travel history and blood picture suggestive of thrombocytopenia were included. Patient demographic details were collected in the prescribed formats.

All the samples of the patients with a history of fever of less than 5 days were tested by NS1Ag ELISA employing Standard Diagnostic Inc kits and the patients with a history of fever beyond 5 days were tested by Dengue IgM MacELISA which was provided by National Institute of Virology, Pune. The tests were performed as per the manufacturer's guideline. The serum samples were stored at 4°- 8° C, but when longer duration of storage was required, it was stored at -20° C. The results were recorded properly and sent to the patients and the concerned authorities.

The test results and other epidemiological variables were put in a proforma for analysis of the results.

### RESULTS

From the six years study we found that the prevalence of Dengue was highest in 2012 (47%) and lowest in 2014 (10%). Highest sample load was seen in 2016 and lowest in 2014. Sample wise ELISA test is shown in **Table 1**.

**Table 1** Seropositivity for Dengue from 2012-2017

Year	NS1Ag ELISA			IgM ELISA			Total		
	Sample tested	Positive	%	Sample tested	Positive	%	Sample tested	Positive	%
2012	2100	1225	58.3%	1017	307	30.2%	3117	1532	49.2%
2013	7553	2041	27%	1976	976	49.4%	9529	3017	32%
2014	1173	51	4.3%	327	46	14.1%	1500	97	6.5%
2015	1959	1648	84.1%	1251	874	69.9%	3210	2522	78.6%
2016	10672	6157	57.7%	3953	1686	42.7%	14625	7843	53.6%
2017	5411	2476	45.8%	2862	910	32%	8273	3386	41%

The age distribution of the cases is discussed in **Table 2**. As is clear from the table we have found that in all the years, males patients were more than the female patients.

Commonest age-group of the affected patients was between 25- 34 years of age.

**Table 2** Age wise distribution of positive dengue cases

Age group in years	2012		2013		2014		2015		2016		2017	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
0-5	5	12	20	11	2	5	35	21	75	64	12	8
6-14	8	2	11	14	8	11	151	77	199	152	53	20
15-24	47	36	128	77	10	12	348	201	1126	526	723	174
25-34	292	99	555	262	6	10	520	277	1270	603	750	421
35-44	570	129	671	384	3	2	270	148	860	539	206	119
45-54	108	68	320	287	9	5	183	129	281	209	128	197
>55	104	52	218	59	6	8	102	60	1009	930	421	154
Total	1134	398	1923	1094	44	53	1609	913	4820	3023	2293	1093

**Table 3** Shows the district wise distribution of the Dengue cases in different districts of Assam. It was observed that the highest number of cases of Dengue belonged to the

Kamrup (Metro) district followed by Kamrup (Rural) in all the years. From the two districts of Dibrugarh and Dima Hasao no samples were received.

**Table 3** District-wise distribution of positive dengue cases

Sl. No.	DISTRICT	2012	2013	2014	2015	2016	2017
1	Baksa	18	28	6	16	105	129
2	Barpeta	16	29	8	41	112	93
3	Bongaigaon	16	7	2	11	21	14
4	Cachar	4	2	2	2	6	4
5	Chirang	6	6	0	2	1	4
6	Darrang	18	33	13	33	80	155
7	Dhemaji	0	9	0	9	10	15
8	Dhubri	10	14	3	17	56	44
9	Goalpara	10	3	2	10	22	41
10	Golaghat	4	3	0	7	12	9
11	Hailakandi	0	5	0	1	1	0
12	Jorhat	4	3	0	4	10	5
13	Kamrup Rural	161	121	13	133	452	365
14	Kamrup Metro	1098	2490	29	1871	6150	1459
15	Karbi Anglong	2	2	0	12	51	10
16	Kamrimganj	4	2	0	4	2	3
17	Kokrajhar	0	0	1	8	15	365
18	Lakhimpur	33	10	0	23	25	27
19	Morigaon	3	10	3	17	30	58
20	Nagaon	12	20	2	48	102	75
21	Nalbari	34	78	2	50	136	120
22	Sonitpur	4	6	0	18	52	27
23	Tinsukia	0	0	0	1	0	3
24	Sibsagar	4	3	0	1	10	7
25	Udalguri	7	7	9	24	26	32
26	Other States	64	124	2	159	356	322
	Total	1532	3017	97	2522	7843	3386

## DISCUSSION

Dengue is emerging as a major public health problem in India. As with other states in India the occurrence of Dengue cases in Assam too is seen to be more in the urban and semi-urban areas.<sup>6-13</sup> Dengue is spreading rapidly and becoming established in Assam, owing to socio-economic and developmental changes, with a dramatic increase in unplanned urbanization, population movement, lack of proper waste management and inadequate vector-control measures. Our study shows that it has come to affect a large populace in the State for the past six years. Subsequently, there was a significant increase in 2012 and 2013 with 1058 and 4526 cases and five and two deaths respectively. But, it decreased in 2014 with 85 cases and no death. Again there was a significant increase in 2015, 2016 and 2017 with 1076, 6157 and 5016 cases respectively. Of the total confirmed cases for each year in Assam, the majority (70–90%) were reported in Guwahati. In 2013, 91% (4121/4526) of the total reported dengue cases were reported in Guwahati alone. The cases were, however, unevenly distributed in different zones of Guwahati, with large concentrations in the East zone and Capital zone. A few confirmed cases have also been reported from other district towns (Dibrugarh, Tinisukia, Lakhimpur, etc.) supported by serological evidence for circulating strains of dengue virus. Cases were reported mostly from those places where people harvest rain water and often leave tyres, drums and canisters out in the open. The actual disease burden is estimated to be much higher, with many cases undiagnosed and additional cases reported in public/private sectors.

Serological testing for Dengue was first started in GMCH in 2010. Since then the sample load has been growing with fluctuant positivity rates. However an encouraging trend in health seeking behavior which we noticed was that majority of the samples over the six years from 2012-2017 could be tested for Dengue NS1Ag implying that the patients reported early to the hospital (i.e. before five days fever). The commonest age group affected in all the years was between 25-34 which is the most economically productive age-group. A male preponderance seen in this study can be attributed to the fact that most women tend to stay indoors while males are the ones to be more outdoors and mobile for work.

Incidence of Dengue in Assam has been documented in many studies.<sup>2-4,14-18</sup> In our study we have seen that the Kamrup (Metro) district has reported the highest number of cases in all the years. An interesting finding of this study is the occurrence of Dengue in districts that were unaffected in previous years (**Table 3**) which can be attributed to increase in long-distance travel, population growth and urbanisation, lack of sanitation, ineffective mosquito control etc.

Poor economic condition and deplorable conditions of living of the people in the country is a hindrance in the control of Dengue in spite of several efforts from the government and NGOs. Misconceptions and wrong beliefs are common, which increases the gap between knowledge and practice in the public, ultimately leading to diseases that can be otherwise controlled by public awareness.

## CONCLUSION

Dengue has remained a persistent problem in Assam with the increasing distribution range of *Aedes aegypti*. There is a need of identification of high-risk areas, vector incrimination and seasonal infectivity of dengue so that future outbreaks can be avoided by targeted interventions. Surveillance for detection of Dengue infections, monitoring of vector activity and initiation of vector control measures should be ensured so as to prevent disease transmission in the high risk zones. The control of *Aedes* mosquitoes in Assam is very challenging and requires community involvement. Destroying the breeding grounds of mosquitoes through an intense public campaign, proper solid waste disposal, improved water storage practices, including covering containers, to prevent access to egg-laying female mosquitoes, supplying medicated mosquito nets in affected areas, protecting oneself from mosquito bites using clothes with long sleeve and mosquito repellent, educating the people on the basics of health and hygiene are a simple yet very effective way of minimizing the impact of Dengue in Assam. In the absence of a licensed vaccine or specific drugs, the containment of spread of the vector and the disease is still important.

**Contribution of Authors:** All authors declare that: (1) The article is original with author(s) and does not infringe any copyright or violate any other right of any third party. (2) The article has not been published (whole or part) elsewhere, and is not being considered for publication elsewhere in any form, except as provided herein. (3) All author(s) have contributed sufficiently in the article to take public responsibility for it and (4) All author(s) have reviewed the final version of the above manuscript and approved it for publication. The contributions were made as: Dr. Dina Raja Concept, study design, data collection, data arrangement, statistical analysis, manuscript writing; Dr Vaishali Sarma, Collect the data, review the manuscript; Dr Parasmitta Das and Dr. Shalini Goldar: Interpret the table and graphs, Draft writing, review the manuscript; Dr. Chimanjita Phukan: Concept, Study Design, Draft writing, Review Manuscript.

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## ORIGINAL RESEARCH PAPER

# A study on isolation and identification of bacterial agents responsible for postoperative wound infection

Sarma MC<sup>1</sup>, Das DK<sup>2</sup>

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### ABSTRACT

**Introduction:** The term post operative wound infection, also known by the term surgical site infection (SSI) is as old as the beginning of surgery. The majority of post operative wound infection (SSI) become apparent within 30 days of an operative procedure and most often between 5<sup>th</sup> and 10<sup>th</sup> post operative days. **Materials and methods:** This was a hospital based observational, descriptive study carried out on 2685 SSI wound samples were included in the present study collected from General Surgery, Orthopedic, Obstetrics and Gynaecology Departments. **Results:** In the present study in the clean wound category with no obvious source of contamination, 65.8% of the cultured infected wounds were of monomicrobial etiology. The isolates when compared with the duration of surgery, it was found that with longer durations of surgery, the wound was infected with polymicrobial agents. The incidence of Klebsiella, E.coli and Pseudomonas increased with longer durations of surgery. This suggests that the organisms might be transferred to the wound by prolonged contact with the operating staff and equipment, as airborne spread of the Gram negative organisms is rare. **Conclusion:** The present study has enlightened the relationship between SSI, preoperative hospitalization and duration of surgery. There was increase in the incidence of infection, in patients with longer preoperative hospitalization and longer durations of surgery. There was an increase in poly-microbial etiological agents in these cases. Klebsiella was found to be the main etiological agent followed by E. coli, Pseudomonas, Coagulase negative staphylococci, etc.

**Keyword:** Surgical site infection (SSI); polymicrobial agents; cultures positive; cultures negative; coagulase positive; coagulase negative.

### INTRODUCTION

The term post operative wound infection, also now by the term surgical site infection (SSI)<sup>1</sup> is as old as the beginning

of surgery. Survey on post operative wound infection (SSI) by different workers show that the incidence is still alarming which frightens both surgeons and patient.<sup>2, 3</sup>

The majority of post operative wound infection (SSI) become apparent within 30 days of an operative procedure and most often between 5<sup>th</sup> and 10<sup>th</sup> post operative days. However, where a prosthetic implant is used, infection affecting the deeper tissues may occur several month after the operation.<sup>4,5,6</sup> Altimeter stated that the principal organisms of SSI were staphylococcus (both coagulase positive and negative) Escherichia coli, proteous, klebsiella, pseudomonas, bacteroides, streptococcus and Clostridium perfringens. Since last 25 year,<sup>7,8,9</sup> the incidence of wound infection due to gram negative organisms is increasing though, staphylococcal infection was more common earlier.<sup>10</sup>

The C.D.C. definition describes three level of post operative wound infection (SSI)

- a) Superficial incisional, affecting the skin and subcutaneous tissue.
- b) Deep incisional affecting the facial or muscle layers.
- c) Organ or space infection, which involves any part of the anatomy other than the incision that is opened or manipulated during the surgical procedure, for example joint or peritoneum.

This paper has aimed to isolate and identify the bacterial agents

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### Address for correspondence:

<sup>1</sup>Assistant Professor

Dept. of Microbiology

FAAMC, Barpeta

**Mobile:** +919864043467

<sup>2</sup>Associate Professor (**Corresponding Author**)

Dept. of Microbiology

Gauhati Medical College, Guwahati

**Email:** drdipakdad606@gmail.com

**Mobile:** +919435474891

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responsible for postoperative wound infection (SSI).

## MATERIALS AND METHODS

A total of 2685 S.S.I. wound sample were included in the present study. It was carried out in the Department of, Microbiology, Gauhati Medical College and Hospital for a period of one year. The materials were obtained from patients in the General Surgery, Obstetrics & Gynaecology and Orthopaedic Departments of GMCH, who had undergone operations and had developed Signs and Symptoms of post-operative wound infections. Cases of Clean and Clean contaminated surgeries are included for the study, whereas procedures in which healthy skin was not incised such as opening of an abscess, burn injuries and donor sites of split skin grafts, contaminated and dirty surgeries are excluded from study samples.

### Collection and transportation of material

The wounds were examined for suggestive Signs/Symptoms of infection in the post operative period, during wound dressing or when the dressings were soaked, until the patient was discharged from the hospital and also in the Out-patient department after discharge. All the specimens collected were transported immediately to the laboratory for further processing. The Nutrient broth and Robertson's cooked meat broth (RCMB) were incubated at 37° C.

**Methods:** The samples collected were processed as follows

- Direct microscopic examination of gram stained smear. The smear was screened for pus cells, the gram reaction, morphology, arrangement and number of types of the organisms were noted.
- Inoculation of the samples onto different culture media for aerobic and anaerobic onto plates of MacConkey agar and 5% Sheep blood agar.
- Preliminary identification.
- Bio-chemical tests.

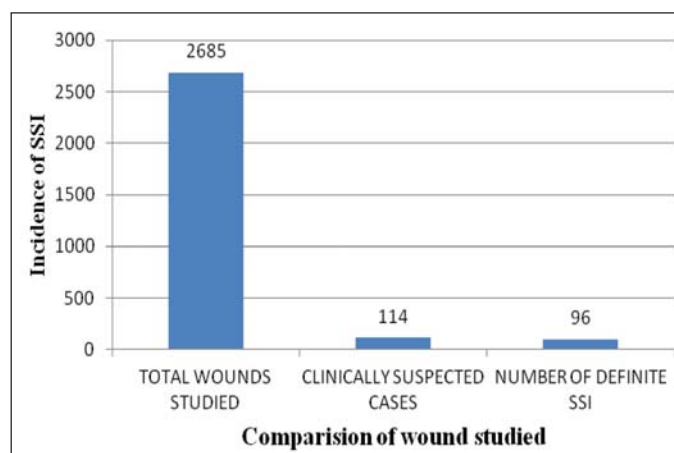
## RESULTS

The following results were made from the study.

**Table 1** Age and sex distribution of cases

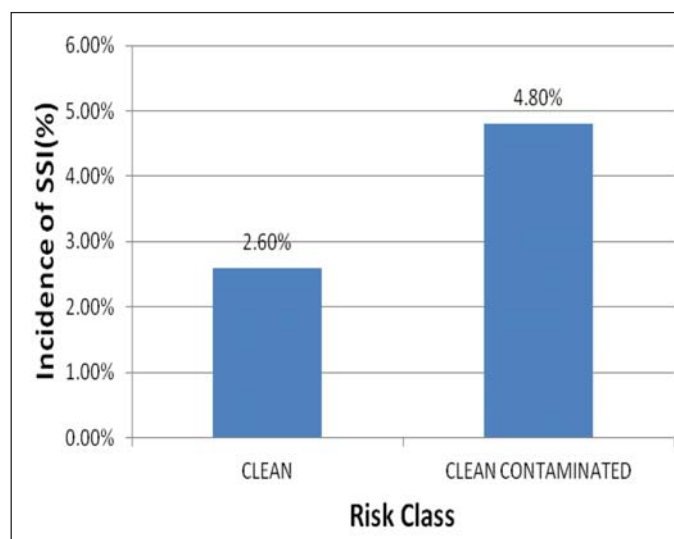
Age Group (in Years)	Total No. of Cases Surgeries Performed	Male	Female
0-10	28	21	7
11-20	175	134	41
21-30	526	439	87
31-40	752	588	164
41-50	711	622	89
51-60	348	246	102
Above 60	93	74	19
<b>Total</b>	<b>2685</b>	<b>2124</b>	<b>561</b>

**Table 1** Shows that maximum number of samples 752(28%) were 31-40 years, followed by 711(26.5%)- 50 years and 93(3.5%) samples were above the age of 70 years. Male and female ratio found to be 4:1.



**Figure 1** Incidence of SSI

**Figure 1** depicts out of the 2685 cases with surgical wounds, 114 cases (4.2%) were suspected to be clinically infected. Amongst 114(4.2%) infected wounds, 96(3.6%) were found culture positive and were considered definite cases of surgical site infection.



**Figure 2** Comparison of incidence of SSI according to risk class

**Figure 2** depicts out of the 1471 operations included in the clean wound category, 38 cases (2.6%) were infected. The incidence of wound infection was significantly high in the clean contaminated wounds, with 58 cases (4.8%) being infected in 1214 surgeries.

**Table 2** shows, out of the 50 wounds clinically suspected to be infected and studied in the clean wound category, 38(76%) were culture positive. In the 64 clinically infected cases of the clean contaminated category, 58



cases (90.6%) were culture positive for various organisms. 18 samples (15.8%) of the 114 samples studied were cultures negative. Organisms in all the

positive cultures were identified as strict aerobe and facultative anaerobe where as none could be identified as strict anaerobe.

**Table 2** Aerobic culture positivity in the wound studied

Risk class		Clinically Infected		Culture Positive		Culture Negative	
	No.	No.	%	No.	%	No.	%
Clean	1471	50	3.4	38	76	12	2.4
Clean Contaminated	1211	64	5.3	58	90.6	6	9.4
<b>Total</b>	<b>2685</b>	<b>114</b>	<b>4.2</b>	<b>96</b>	<b>84.2</b>	<b>18</b>	<b>15.8</b>

**Table 3** Comparison of wounds and culture positive cases with pre-operative hospitalization

Pre-operative Hospitalization	Surgeries Performed		Culture Positive cases	
	No	%	No	%
Upto 1 day	1546	57.7	21	1.3
2 days to 1 week	683	25.4	43	6.2
More than 1 week	456	16.9	32	7.01

The above table (**Table 3**) shows, there is an appreciable increase of surgical site infection in patients with a longer pre-operative hospital stay. Among the 1546 patients (57.71%) who had a preoperative hospitalization of upto 1 day and the infection rate was 1.3%. The rate of infection showed an increase to 6.2% in the 683 patients (25.4%) hospitalized 2 to 7 days before surgery. The rate further increased to 7.01% in the 456(16.9%) patients admitted for more than 7 days prior to surgery.

**Table 4** Comparison of wound and culture positive cases with duration of surgery

Duration of surgery (minutes)	Surgeries Performed		Culture Positive cases	
	No	%	No	%
0-60	1865	69.5	46	2.5
61-120	691	25.7	33	4.8
Above 121	130	4.8	17	13.07

The above table(**Table 4**) shows, the duration of surgery in majority of the cases was less than 1 hour. The infection rate showed a marked increase with longer duration of surgery. In 1865 cases which took less than 1 hour, 46 cases (2.5%) were infected. In 691 cases which took 1 hour to 2 hour, 33 cases (4.8%) were infected. Among the 30 cases which took more than 2 hours 17 cases (13.07%) were infected.

**Table 5** Organisms isolated in 96 SSI

Organism	No.	%
Klebsiella species	35	22.3
Staphylococcus aureus	31	19.4
E.coli	24	15.3
Pseudomonas	20	12.7
Cons	18	11.5
Acinetobacter	07	4.5
Proteus species	07	4.5
Diphtheroids	05	3.2
Citrobacter	03	1.9
Enterococci	02	1.3
S.pyogenes	02	1.3
Candida	03	1.9
<b>Total</b>	<b>157</b>	<b>—</b>

## DISCUSSION

One of the most known important factors influencing the incidence of post operative wound infections is wound contamination class. Among the Clean wounds, which accounted for more than half the number of cases, the rate of infection was only 2.6%. But in Clean contaminated cases, the rate of infection almost doubled to 4.8%. probably because of profound influence of endogenous contamination.

The present study confirms the understanding that there is a gradual rise in incidence of wound infection as age advances. The incidence showed a gradual rise from 2.5% in the 21-30 age group to 8.6% in patients more than 60 years. The finding is similar with study carried out by Cruse and Foord.<sup>4,11</sup>

The surgical patient is colonized by microorganisms, during his stay in the hospital. Longer preoperative hospitalization is associated with wound infection. In present study, the incidence

was 1.3% in the patients hospitalized up to 1 day, 6.2% in patients hospitalized for 2 days to 1 week and 7.01 % in patients hospitalized for more than a week. It was consistent with study of Anvikar.<sup>12</sup>

In the present study, majority of the surgical procedures lasted for less than 1 hour and the infection rate among these cases was 2.5%. The rate roughly doubled to 4.8% when the duration of the procedure was 1 hour to 2 hours, and trebled to 13.07%, in procedures lasting for more than 2 hours. This finding is in consistent with study carried out by Cruse and Foord.<sup>11</sup>

The increased incidence of infection may be due to contamination of the wound, by bacteria sedimented from exogenous sources over the duration of time. The length of incision is usually less, in surgeries which take a shorter duration, than in longer surgeries where the area exposed to the environment is more due to longer incisions and also a larger degree of damage to tissues and local disruption.

In the present study, on direct microscopy 84.2% samples yielded growth on culture and this finding was in consistent with study of Anvikar et al.<sup>12</sup>

There is a change in the bacterial etiology of surgical infections from time to time. A century ago, the most feared and frequent pathogen was *Streptococcus*, twenty years ago the Coagulase positive staphylococcus was the principal offender, Gram negative bacilli are now replacing staphylococcus.<sup>3,13,14</sup>

The present study shows the emergence of Gram negative bacilli accounting for 61% of the isolates, as the principal offenders of surgical wound infection. In the present study anaerobic organisms were not isolated on culture, probably because the patients were treated with prophylactic and therapeutic antibiotics against anaerobes.

In the present study of 114 clinically suspected SSI, 96 yielded aerobic bacterial growth accounting for a total of 157 organisms. Mono-microbial isolates were encountered in 52(54.4%) of the wounds, 44 wounds (45.8%) yielded polymicrobial agents, Gram positive and Gram negative organisms were frequently involved in the mixed infections. *Staphylococcus aureus* and *E.Coli* were the commonest combination present in 7 cases (15.9%). Similar spectrum of organisms was observed by Giacometti, et al, who isolated 1060 bacterial strains from 614 individuals.<sup>11</sup>

The clean wound category with no obvious source of contamination, 65.8% of the cultured infected wounds were of monomicrobial etiology. The isolates when compared with the duration of surgery, it was found that with longer durations of surgery, the wound was infected with polymicrobial agents, The incidence of *Klebsiella*, *E.coli* and *Pseudomonas* increased with longer durations of surgery. This suggests that the organisms might be transferred to the wound by prolonged contact with the operating staff and equipment, as airborne spread of the Gram negative organisms is rare.<sup>15,16</sup>

## CONCLUSION

The present that was conducted in Gauhati Medical College Hospital, Guwahati has enlighten the relationship between SSI, preoperative hospitalization and duration of surgery. There was increase in the incidence of infection, in patients with longer preoperative hospitalization and longer durations of surgery. There was an increase in poly-microbial etiological agents in these cases. *Klebsiella* was found to be the main etiological agent followed by *E Coli*, *Pseudomonas*, Coagulase negative staphylococci etc. It was observed that the gram negative bacilli were the main offenders in Clean contaminated operations, in patients with longer preoperative hospitalization and in surgeries with increased duration. Based on the above observations preventive and prophylactic measures can be enhance to lower down the incidence of post operative wound infection (SSI)

**Conflict of interest:** None declared.

**Ethical clearance:** Taken.

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## ORIGINAL RESEARCH PAPER

# A study of the renal profile in ART naive HIV/AIDS patients

Baruah R<sup>1</sup>, Baishya H<sup>2</sup>, Baruah SK<sup>3</sup>

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### ABSTRACT

**Background:** As HIV/AIDS has emerged to be the first modern pandemic with ever increasing prevalence globally, the present study was undertaken to study the renal profile in patients living with HIV/AIDS, not started on ART. **Materials and methods:** This was a hospital based observational study where 277 cases were studied in details with the aims and objectives of studying the renal manifestations in ART naïve patients with HIV/AIDS and its relationship with CD4 counts. A detailed history, clinical examination and relevant investigations were done in patients above 15 yrs of age who were not on ART. **Results:** Out of 277 seropositives, 40 had proteinuria (14.44%) on urine examination. The mean serum creatinine of the total study population was found to be  $0.92 \pm 0.83$  mg/dl while 14 cases (5%) had serum creatinine more than 1.5mg/dl. A decrease in eGFR ( $<60$  ml/min/1.73m<sup>2</sup>) was seen in 28 (10.1%) cases. Out of 178 cases with CD4 count more than 200 cells/mm<sup>3</sup>, renal dysfunction was found in 12 cases (6.7%), whereas the cases with CD4 count less than or equal to 200 cells/mm<sup>3</sup>, 19 out of 99 cases (19.2%) had renal dysfunction which is statistically significant. **Conclusion:** In the present study, which included ART naive patients with HIV/AIDS, predominant renal involvement was in the form of proteinuria followed by raised serum creatinine levels and reduced eGFR. A negative correlation was found between renal dysfunction and CD4 counts.

**Keywords:** HIVAN (Human immunodeficiency virus associated nephropathy); Renal dysfunction in HIV; CD4 count.

### INTRODUCTION

As the fourth leading cause of death around the world and the first leading cause of death in Africa, HIV/AIDS continues to affect 36.7 million people worldwide.<sup>1</sup> The national adult HIV prevalence in India is 0.26%. The total number of People Living with HIV (PLHIV) in India is estimated at 21.17 lakhs

of which children account for 6.54% in 2015.<sup>2</sup>

The clinical consequences of HIV infection encompass a spectrum ranging from an acute clinical syndrome associated with primary infection to a prolonged asymptomatic stage to advanced disease. The spectrum of illnesses changes as the CD4+ T cell count declines.

Diseases of the kidney or genitourinary tract may be a direct consequence of HIV infection, due to an opportunistic infection or neoplasm, or related to drug toxicity. In the pre-ART era, HIV associated nephropathy (HIVAN) was characterised by rapid progression to end-stage renal disease (ESRD) leading to the need for dialysis. With the advent of ART, the natural course of disease has changed increasing the importance of prompt diagnosis and treatment. Despite improved outcomes among persons living with HIV who are treated with antiretroviral therapy, they remain at increased risk for acute and chronic kidney diseases and are important contributors to morbidity and mortality in PLHIV.

Patients with HIVAN typically present with heavy proteinuria and rapidly progressive kidney failure and definitive diagnosis requires kidney biopsy, which reveals focal glomerulosclerosis and tubular microcyst formation with tubulointerstitial inflammation and fibrosis.<sup>3</sup> HIV type 1 (HIV-1) infected

### Address for correspondence:

<sup>1</sup>Associate Professor

**Mobile:** +919435015669

**Email:** baruah\_rumi@yahoo.co.in

Department of Anaesthesiology

Fakaruddin Ali Ahmed Medical College and Hospital, Barpeta

<sup>2</sup>Registrar (**Corresponding author**)

**Mobile:** +919435252153

**Email:** hitakalpa12@gmail.com

<sup>3</sup>Professor and Head

Department of Medicine, Gauhati Medical College and Hospital, Guwahati, Assam and India

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patients are at a greater risk of developing acute and chronic renal diseases. HIV-1 associated nephropathy is now the 3<sup>rd</sup> leading cause of end stage renal disease in 20-64 years of age in the United States. These patients typically have proteinuria followed by a reduction in the glomerular filtration rate (GFR) that progresses to end stage renal disease in few weeks or months. Overall microalbuminuria is seen in ~20% of untreated HIV infected patients, significant proteinuria is seen in closer to 2%. The presence of microalbuminuria has been associated with an increase in all-cause mortality rate.<sup>4</sup>

Absolute CD4 counts are accepted as the best indicator of immunologic competence of patients with HIV infection and they are an indirect reflection of HIV viral load and activity. The CD4+ T cell count in patients with HIVAN is usually <200 cells/mm<sup>3</sup>, but has been reported in patients with higher counts. Lower CD4 counts is also associated with increased risk of AKI in HIV infected patients.<sup>5</sup>

This paper has aimed to study the incidence of renal dysfunction in ART naïve HIV/AIDS patients, different types of renal dysfunction and to find the correlation between renal dysfunction and CD4 count.

## MATERIALS AND METHODS

**Study location:** This study was conducted at tertiary care hospital. 277 cases were collected from the ART Plus Centre, Department of Medicine and Nephrology departments (both outpatient and inpatient).

**Study design:** This was a hospital based observational study conducted between 1<sup>st</sup> July 2016 to 30<sup>th</sup> June 2017. Approval was taken from the institutional ethics committee. Informed written consent was taken from all the patients included in the study.

**Inclusion criteria:** (i) HIV positive adult patients (as per NACO guidelines) above 15 years; (ii) Patients not on ART.

**Exclusion criteria:** (i) All HIV positive children below 15 years (as per NACO guidelines); (ii) Patients with pre-existing renal parenchymal disease due to diabetes, long-standing hypertension, cardiac failure and collagen vascular disease; (iii) Patients who are on antiretroviral therapy.

Patients with serum creatinine  $\geq 1.5$  mg/dl were labelled as having renal dysfunction. Patients with renal dysfunction and/or spot proteinuria  $> 1+$  or 24-h urinary protein  $\geq 500$ mg were classified as having renal involvement.<sup>6</sup> The Cockcroft and Gault equation which estimates creatinine clearance on the basis of serum creatinine level, age, sex and weight was used. The formula is as follows:

$$eCrCl = \frac{140 - \text{age( yrs )} \times \text{weight ( kg )}}{72 \times \text{s. creat ( mg/dl )}} \quad (\times 0.85 \text{ for females})$$

## RESULTS

### 1. Incidence of Proteinuria

Out of 277 seropositives, 40 had proteinuria (14.44%) on urine examination. Of these, 36 had  $\geq 1+$  spot proteinuria, 2 each had  $\geq 2+$  and  $\geq 3+$  proteinuria (**Table 1**). The mean 24 hour urinary protein estimation done in these cases (n=40)

was found to be  $856.02 \pm 372.88$  mg/day. Proteinuria  $> 1$ g/day was found in 4 cases (10%).

**Table 1** Incidence of proteinuria

RANGE OF PROTEINURIA	NUMBER OF CASES	PERCENTAGE(%)	Mean 24 hours Urinary protein (9mg/d)
$\leq 1+$	36	12.99	748.13 $\pm$ 98.3
$\leq 2+$	2	0.72	1374 $\pm$ 246.07
$\leq 3+$	2	0.72	2280 $\pm$ 113.14

### 2. Analysis of serum creatinine

The mean serum creatinine of the total study population was found to be  $0.92 \pm 0.83$  mg/dl. When serum creatinine  $\geq 1.5$ mg/dl was considered as renal dysfunction, the mean creatinine levels of that group (14/277) was found to be  $3.05 \pm 2.92$  mg/dl (95%CI=1.37-4.74), which is statistically significant ( $p < 0.0001$ ) (**Table 2**).

**Table 2** Analysis of serum creatinine

CATEGORY	MEAN CREATININE
TOTAL STUDY GROUP	$0.92 \pm 0.83$ mg/dl
CASES WITH RENAL DYSFUNCTION	$3.05 \pm 2.92$ mg/dl

### 3. Analysis of creatinine clearance

The total number of cases with decreased creatinine clearance ( $< 60$ ml/min/1.73m<sup>2</sup>) was seen in 28(10.1%) cases. CKD stage G3 (moderate to severe renal dysfunction) i.e, creatinine clearance between 30- 59 ml/min/1.73m<sup>2</sup> was seen in 23 cases. However, stage G4 (Cr cl =15-29ml/min/1.73m<sup>2</sup>) was seen in 7 cases and G5 (Cr cl  $< 15$  ml/min/1.73m<sup>2</sup>) was seen in 1 case only (**Table 3**).

**Table 3** Analysis of creatinine clearance

CREATININE CL (ML/MIN)	CKD STAGE	NUMBER OF CASES	PERCENTAGE(%)
$\geq 90$	G1	160	57.8
60-89	G2	86	31.0
30-59	G3	23	8.3
15-29	G4	7	2.5
$< 15$	G5	1	0.4

(Range=5-252.10ml/min, mean=103.10ml/min)

### 4. Renal dysfunction in relation to CD4 counts

Out of 178 cases with CD4 count more than 200 cells/mm<sup>3</sup>, renal dysfunction was found in 12 cases (6.7%) (**Table 4a**). Whereas of the 99 cases with CD4 count less than or equal to 200 cells/mm<sup>3</sup>, 19 cases (19.2%) had renal dysfunction which is statistically significant (P value=.01; relative

risk=0.602; 95%CI=0.38-0.94). The mean CD4 count in patients with renal involvement was  $227.2 \pm 233.63$  cells/mm<sup>3</sup> (**Table 4b**) while in those without renal involvement was  $331.7 \pm 223.4$  cells/mm<sup>3</sup> (P value <.0001; relative risk=2.87; 95% CI= 2.07-3.81).

**Table 4** Renal dysfunction in relation to CD4 counts

**Table 4(a)**

CD4 COUNT	TOTAL NO. OF CASES	CASES WITH RENAL DYSFUNCTION(%)
>200 cells/mm <sup>3</sup>	178	12 (6.7%)
≤200 cells/mm <sup>3</sup>	99	19 (19.2%)

(P value=.01)

**Table 4(b)**

CATEGORY	MEAN CD4 COUNT
With renal involvement	$227.2 \pm 233.63$ cells/mm <sup>3</sup>
Without renal involvement	$331.7 \pm 223.4$ cells/mm <sup>3</sup>

(P value<.0001)

## DISCUSSION

In the present study, out of 277 seropositives, 40 had proteinuria (14.44%) on urine analysis. Of these, 36 had ≥1+ spot proteinuria, 2 each had ≥2+ and ≥3+ proteinuria. This is consistent with the study by Gupta V et al<sup>6</sup> in North India who reported 58 patients out of 392 ART naïve cases to have proteinuria (14.79%). Similarly, Varma P. et al<sup>7</sup> also reported 25/142 (17.6%) HIV positive cases to have proteinuria or abnormal urinary sediment. Janakiraman H et al<sup>8</sup> studied 104 HIV positive patients, albuminuria was observed in 29 (27%) patients. Similarly, Prakash J. et al,<sup>9</sup> reported proteinuria of 1+ or more in 112 (38.2%) patients in his study. The discrepancy in the incidence of proteinuria with the present study was probably due to the difference in sample size. The mean 24 hour urinary protein in the cases with spot proteinuria (40/277) was found to be  $856.02 \pm 372.88$  mg/day, in the present study. However, in the study of Gupta V. et al<sup>6</sup> the mean 24 hour proteinuria was found to be  $1561 \pm 906$  mg/day in patients with proteinuria (n=130). The difference with the present study might be due to difference in sample size and inclusion of patients on ART in his study. No patient in the present study had nephrotic range proteinuria. Proteinuria > 1g/day was found in 4 cases (10%) in the present study which was similar to Prakash J. et al,<sup>9</sup> who found 16(14.2%) patients to have proteinuria of more than 1g/24h.

The mean serum creatinine of the total study population was found to be  $0.92 \pm 0.83$  mg/dl. When serum creatinine >1.5mg/dl was considered as renal dysfunction, the mean creatinine levels of that group (14/277) was found to be  $3.05 \pm 2.92$  mg/dl, which was higher than the total study population. In a

study by Atta MG et al,<sup>10</sup> the patients with biopsy proven HIV-associated nephropathy and not on ART had a significantly higher mean creatinine level ( $7.8 \pm 2.9$ mg/dl) at the time of biopsy than those on ART. This was similar to the study by Gupta V et al<sup>6</sup> where among a group of 392 ART naïve patients, 74(18.9%) had renal involvement. Patients with renal dysfunction had a mean serum creatinine of  $4.60 \pm 3.17$  mg% (range 1.7-10.5).

In the present study, the total number of cases with moderate to severe renal dysfunction was found to be 23 (8.3%). However, Cr cl =15-29ml/min/1.73m<sup>2</sup> was seen 2.5% and Cr cl <15 ml/min/1.73m<sup>2</sup> was seen in 0.4%. Overall, patients with creatinine clearance <60ml/min were 28(10.1%). Similarly, the prevalence of CKD in Chinese patients was found to be 5.6% by Cheung CY et al.<sup>11</sup>

In the present study, out of 178 cases with CD4 count more than 200 cells/mm<sup>3</sup>, renal dysfunction was found in 12 cases. Whereas of the 99 cases with CD4 count less than or equal to 200 cells/mm<sup>3</sup>, 19 cases had renal dysfunction. The findings is statistically significant. This findings are similar with studies like Janakiraman H. et al, who studied HIV positive patients, and reported that albuminuria was observed. It revealed a significant negative correlation with CD4 count.<sup>8</sup> HLF Kamga. et al also found that creatinine clearance in HIV positive patients with CD4 count below 200 cells/mm<sup>3</sup> was low while serum creatinine levels were higher though it was not statistically significant.<sup>12</sup>

In the present study, the mean CD4 count in patients with renal involvement was  $227.2 \pm 233.63$  cells/mm<sup>3</sup> which was lower than those without renal involvement. The patients with ART naïve HIV-associated nephropathy had a lower mean CD4 count ( $161 \pm 130$  cells/mm<sup>3</sup>) at the time of biopsy.<sup>10</sup> In another recent study the mean CD4 count of ART naïve patients was significantly lower in patients with renal involvement as compared to those without renal involvement ( $180 \pm 154$  vs  $302 \pm 201$  cells/mm<sup>3</sup>).<sup>6</sup>

## CONCLUSION

In the present study, which included ART naïve patients with HIV/AIDS, predominant renal involvement was in the form of proteinuria followed by raised serum creatinine levels. Creatinine clearance and thus GFR is reduced in HIV/AIDS patients and a negative correlation was found between renal involvement and CD4 counts. Although, proteinuria was present in some HIV/AIDS patients in our study population, this parameter alone is not indicative of HIVAN.

**Conflict of Interest:** None declared.

**Ethical Clearance:** Taken.

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## ORIGINAL RESEARCH PAPER

# Inter-canine width as a tool for sexual dimorphism and stature estimation

Singh Rattan<sup>1</sup>, Bhasin Neha<sup>2</sup>, Barwa Jyoti<sup>3</sup>, Das Sanjoy<sup>4</sup>

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## ABSTRACT

**Introduction:** Identification by means of dental tissue is an easy and helpful tool in forensic Odontology. Dental architecture grows in proportion to the human body and shows some positive correlation. Being hard and resistant to adverse conditions makes it very valuable in scientific studies. Since canine has a longer root in the jaw, it makes it a notifiable structure that can be used in research. Hence, among the dental tissues, canine tooth is chosen most often in studies. **Materials and methods:** study was conducted in Department of Forensic Medicine & Toxicology, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, involving 200 subjects (100 males & 100 females) 19 to 24 years of age. Inter-canine width of their maxilla and mandible were measured by manual vernier caliper to determine sex and height; data was analyzed by SPSS software. **Result:** Mean Maxillary and Mandibular Inter-canine width of males was found to be more as compared to females and were statistically highly significant. Sexual dimorphism was more by using Mandibular Inter-canine width as compared to Maxillary Inter-canine width. Percentage accuracy of sex determination was found to be more in Maxillary Inter-canine width. Simple linear regression equations were obtained for predicting height from Inter-canine width. Correlation between Height and Inter-canine width of Maxilla and Mandible was statistically significant in males than females. **Conclusion:** Sexual dimorphism and stature estimation is possible by measuring Inter-canine width. However, better prediction with more accurate height and sex determination requires a combined study of dental tissue along with bones.

**Keywords:** Forensic Odontology; dental tissue; canine; identification.

## INTRODUCTION

Human beings have important characteristics that differ from each other due to uniqueness, and one such feature is the morphology of dentition. It is one of the most durable parts like bone in the body that resist damage under time factors and weather conditions. These unique and strong characteristics of dentition is used for the purpose of research in medico-legal field. An excellent proof of its indestructible property is the presence of teeth in the lower jaw of Tabun man which is approximately about 35,000 years old.<sup>1</sup>

In Human jaw, canine's morphology and structure is such that it is less affected by disease, plaque, abrasion from brushing and is also the least extracted tooth.<sup>2-4</sup> Canine can survive even in a hurricane disaster.<sup>5</sup> In situations, such as flood, earthquakes, cyclones, tsunami etc where body is

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### Address for correspondence:

<sup>1</sup>Assistant Professor (Corresponding author)

**Mobile:** +918076544096

**Email:** dr.rattan.singh2004@gmail.com

<sup>2</sup>MBBS Student

**Mobile:** +917982870981

Himalayan Institute of Medical Sciences, Jolly Grant, Dehradun, Uttarakhand-248140, India

<sup>3</sup>Assistant Professor

Department of Forensic Medicine & Toxicology  
Shri Guru Ram Rai Institute of Medical and Health Sciences,  
Dehradun, Uttarakhand, India

<sup>4</sup>Professor and Head

Department of Forensic Medicine & Toxicology  
Himalayan Institute of Medical Sciences, Jolly Grant, Dehradun,  
Uttarakhand, India

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decomposed and identification becomes difficult then, the odontometric parameters helps in identification of the individual. The most reliable, easy, and less time-consuming method in investigation is the measurement of teeth. It was reported that sexual dimorphism<sup>6,7</sup> and stature estimation from permanent canines and their arch width could be possible. However, using dentition for estimation of stature needs more exploration and with this background, the current study was conducted to establish a relationship between stature, sexual dimorphism and Inter-canine width.

The aims of this study is to find out sexual dimorphism based on Inter-canine width and to find out relationship between Inter-canine width and stature

## MATERIALS AND METHODS

A descriptive cross sectional study was conducted in the Department of Forensic Medicine and Toxicology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Uttarakhand, involving 200 subjects (100 males and 100 females) of age ranging from 19 to 24 years. A written informed consent was duly obtained from all of them, informing about the study, purpose and techniques to be used for the measurements. Only those subjects having normal dental alignment with complete eruption of permanent teeth were included. Subjects having missing teeth, fractured teeth, dental caries, endocrine or any other abnormalities were excluded from the study.

Inter-canine width is defined as the horizontal distance between the two canines. It was measured using a manual Verniercaliper; the subject was asked to open his/her mouth

were placed at the medial borders of right and left canine of both the jaw, then an average value was noted. In order to maintain proper hygiene, after taking these measurements, the tips of Verniercaliper were cleaned before using it on another subject.

For measuring the stature, a stadiometer was used; the subject was asked to stand barefoot in an upright posture with his/her head positioned in Frankfurt plane and with his/her heel, buttocks, scapulae and occiput touching the measuring rod, then by using a movable rod, the reading was taken. To reduce the errors while observing, all the readings were taken twice. The collected data was then analysed using SPSS.

## RESULTS

The mean Inter-canine width of males was more than females in both Mandible as well as Maxilla; they were found to be statistically highly significant. Since, T value between males and females was more in Maxillary Inter-canine width than Mandibular Inter-canine width, hence sexual dimorphism is more in Mandibular Inter-canine width. Also, sex can be differentiated on the basis of Inter-canine width of the subjects as P value is less than 0.05, which is statistically highly significant (**Table 1**).

Percentage accuracy to predict the sex on the basis of Inter-canine width is 62 % in males and 70% in females if using maxilla, 68 % in males and 55 % in females if using mandible.

Correlation between the stature and Maxillary Inter-canine width is more positive and stronger as compared to Mandibular Inter-canine width in total subjects as well as

**Table 1** Independent t test: for sex differentiation from Inter-canine width

Parameter	sex	Mean $\pm$ SD	T value	P value	Level of Significance	% of sexual dimorphism
Maxillary Inter-canine width	M	3.4512 $\pm$ .23568	5.027	.000	Highly significance	5.43 %
	F	3.2980 $\pm$ .19336				
Mandibular Inter-canine width	M	2.7042 $\pm$ .22900	4.466	.000	Highly significance	6.16 %
	F	2.5712 $\pm$ .19036				

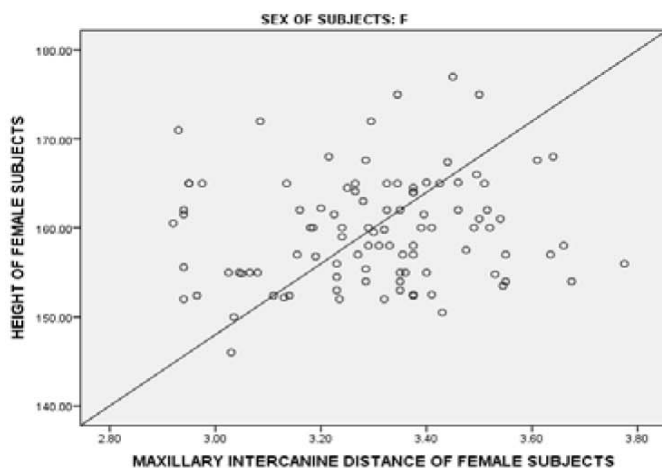
and then the two tips of external jaw of manual verniercaliper were placed at the distal borders of right and left canine respectively for measuring the maximum Inter-canine width (max. Id) and for measuring the minimum Inter-canine width (min. Id), the tips of the external jaw of manual Verniercaliper

male and female subjects individually. They were found to be statistically highly significant in total subjects and male subjects as p value is less than 0.05 but not statistically significant in female subjects as p value is more than 0.05 (**Table 2**).

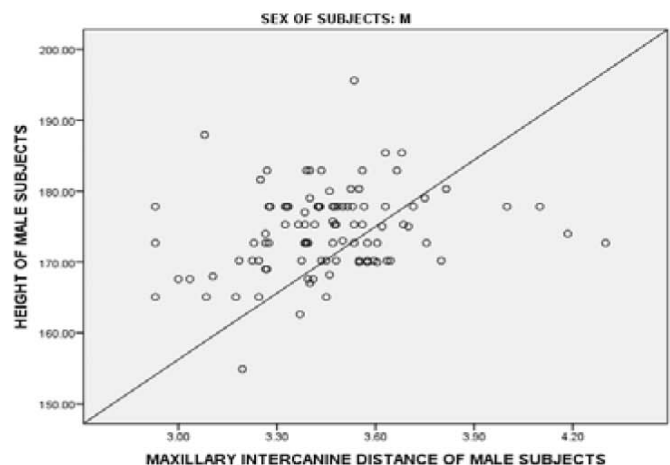


**Table 2** Regression analysis for predicting stature (Y) of subjects (dependable variable) considering Inter-canine width as an independent variable

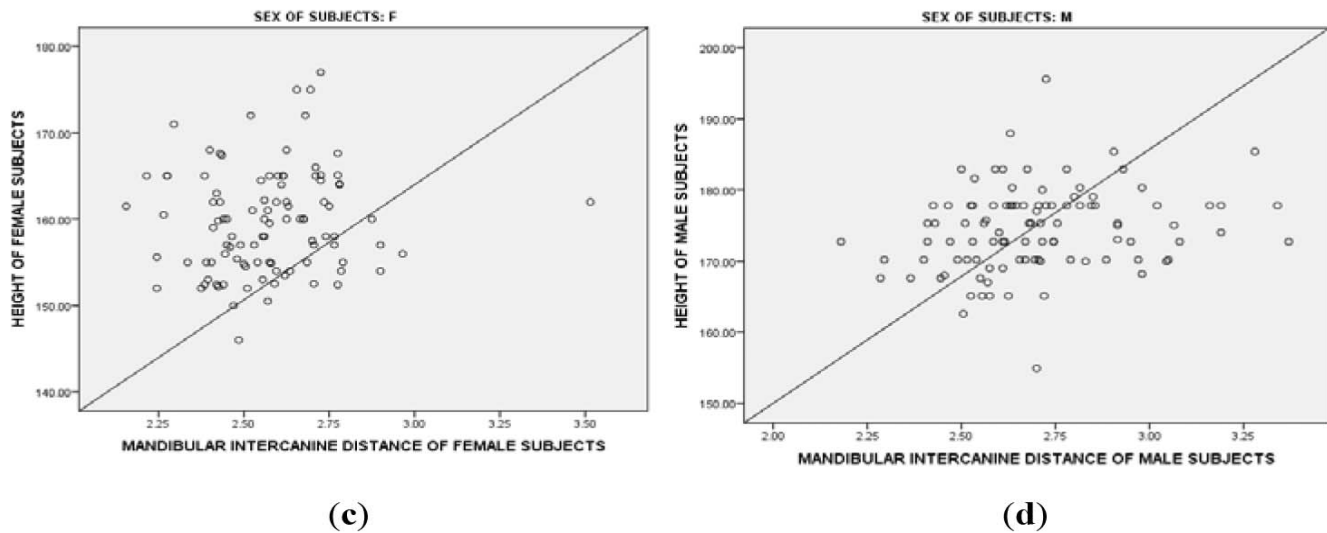
Parameter	Mean	Std. Deviation	Correlation value	P value	R Square	Regression equation
Mean Height of <b>Total</b> Subjects (n= 200 )	167.06	9.48231	.368	.00	.135	Y = 115.525 + 15.270 (maxillary Intercanine width in Total Subjects)
Mean Maxillary Inter-canine width of Total Subjects (n =200)	3.37	.22833				
Mean Height of <b>Total</b> Subjects (n= 200 )	167.06	9.48231	.332	.00	.110	Y = 129.355 + 14.293 (mandibular Intercanine width in Total Subjects)
Mean Mandibular Inter-canine width of Total Subjects (n =200)	2.64	.22037				
Mean Height of <b>Male</b> Subjects (n=100)	174.42	5.90969	.239	.008	.057	Y = 153.706 + 6.003 (maxillary Intercanine width Of male Subjects)
Mean Maxillary Inter-canine width of Male Subjects (n =100)	3.45	.23568				
Mean Height of <b>Male</b> Subjects (n=100)	174.42	5.90969	.217	.015	.047	Y = 159.258 + 5.609 (mandibular Intercanine width in male Subjects )
Mean Mandibular Inter-canine width of male Subjects (n = 100)	2.70	.22900				
Mean Height of <b>Female</b> Subjects (n=100)	159.69	6.00936	.109	.141	.012	Y = 148.563 + 3.373 (maxillary Intercanine width in Female Subjects )
Mean Maxillary Inter-canine width of Female Subjects (n =100)	3.30	.19336				
Mean Height of <b>Female</b> Subjects (n=100)	159.69	6.00936	.097	.168	.009	Y = 115.525 + 15.270 (mandibular Intercanine width in Female Subjects )
Mean Mandibular Inter-canine width of Female Subjects (n =100)	2.57	.19036				



(a)



(b)



**Figure 1** Scatter diagram showing correlation between Inter canine width and stature (a to d)

## DISCUSSION

The present study was conducted for sexual dimorphism using Mandibular and Maxillary Inter canine width, thereafter prediction of stature was done by considering Inter canine width as an independent variable. The mean Mandibular Inter canine width was more in males as compared to females; statistically significant difference was found as p value was less than .05. These findings are consistent with most of the studies<sup>8-17</sup> but inconsistent with study conducted by Dayananda<sup>18</sup> where mean value was more in males but statistically insignificant difference was observed. In the present study, mean Maxillary Inter canine width was more in males as compared to females and statistically significant difference was found between males and females which is consistent with Prakash Chandra Jha<sup>18</sup> and Rao G V<sup>19</sup> but inconsistent with Hamid and Mastooreh<sup>20</sup> where statistically insignificant difference was found. Sexual dimorphism using Mandibular Inter canine width in the present study was found to be 6.61 % whereas a slightly higher percentage was found by Fulwaria Mukesh<sup>21</sup> (13.74 %). The correlation coefficient between Stature and Maxillary inter canine width of the present study was found to be weakly positive (0.368) and a statistically significant relationship was obtained which is consistent with Harshala S Patil's<sup>22</sup> ( $r = 0.493$  and  $p$  value  $< 0.05$ ).

## CONCLUSION

Sexual dimorphism is successfully possible if Inter canine width of Maxilla and Mandible are measured in the jaw. Also, percentage of sexual dimorphism using Mandibular Inter canine width is more than Maxillary Inter canine width. The percentage accuracy to predict the sex, considering Inter canine width is more in females if using Maxilla and more in males if using Mandible. Since, we obtained a positive, weakly strong correlation and not a very high percentage of sex prediction. Hence, there is a need for more research relating to Inter canine width involving a larger population of different age groups. In order to obtain a more reliable, better

and more accurate prediction of stature and sexual dimorphism it suggested to conduct a combined study of dental tissues and bones in contrast to dental issues alone.

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**Conflicts of interest:** None.

**Contribution of Authors:** All authors declare that: (1) The article is original with author(s) and does not infringe any copyright or violate any other right of any third party. (2) The article has not been published (whole or part) elsewhere, and is not being considered for publication elsewhere in any form, except as provided herein. (3) All author(s) have contributed sufficiently in the article to take public responsibility for it and (4) All author(s) have reviewed the final version of the above manuscript and approved it for publication. The contributions were made as: Dr. Rattan Singh: Concept, study design, data collection, data arrangement, statistical analysis, manuscript writing; Neha Bhasin: Collect the data, review the manuscript; Dr. Jyoti Barwa: Interpret the table and graphs, Draft writing, review the manuscript; Dr. Sanjoy Das: Concept, Study Design, Draft writing, Review Manuscript.

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## ORIGINAL PAPER

# Medical students' knowledge about research methodology and impact of research workshops

Deka SJ<sup>1</sup>, Moondra AK<sup>2</sup>, Mahanta Putul<sup>3</sup>

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### ABSTRACT

**Introduction:** It is an open fact that a research is very crucial for development of society. Despite various studies on the benefits of research, there is no fresh study about students' familiarity with principles of research methodology and impact of research workshops in the medical education of India. **Objectives:** In this study, we have aimed to assess undergraduate medical students' knowledge in principles of research methodology and impact of research workshops and about the factors affecting it. **Materials and methods:** In this cross-sectional study, we have investigated 100 randomly selected students who were in their basic science stage of medical studies at Assam Medical College, Dibrugarh in the year 2019. To determine knowledge about principles of research, participants filled a validated and reliable pre-texted questionnaire. The distinctive responses of the students, i.e., their answers to the questions on research principles were collected and analyzed. Linear regression models were applied to predict the score of knowledge of the participants. **Results:** Significant improvement was observed in 82.50% in the mean knowledge score after the workshop and the findings are found to be sensitives (p-value .002). However, attitude score after the workshop remains same (63.75%) even after the workshop. **Conclusion:** Despite limitations of this study, our findings has highlighted low to moderate level of knowledge of undergraduate medical students in principles of research methodology and the important impact of research workshops. These findings can be utilized for future health research planning to improve the situation in the field of medical education, etc.

**Keywords:** Medical education; research impact; ethical issues.

### INTRODUCTION

Health research training on research methodology is an important part of medical education.<sup>1</sup> In recent past, the apprehension about the research activities among medical

students, faculties and researchers working in various medical institutions has increased in South Asia.<sup>1-3</sup> The reasons of this apprehension are multi-factorial including mandatory research publications for professional promotions, elective research assignments and projects given to the students and as part of academic exercises among medicos for presenting papers in conferences and Continuing Medical Education (CME). The aims were moulding of medical curriculum to integrate capacity building for research and holding of workshops on different aspects of conducting research.<sup>2,3</sup>

In view of the present context, it is important to determine the efficacy of each intervention of learning in enhancing the interest and skills of students in health research and to identify those areas necessitating development to meet up the new challenges.

With this backdrop, this study was conducted among medical students to determine the impact of a workshop on research methodology, as a short-term intervention, on their knowledge and attitudes about health research before and after attending a training session on research proficiencies, conducted in the college.

### MATERIALS AND METHODS

In this cross-sectional study, 100 randomly selected students

#### Address for correspondence:

<sup>1</sup>Associate Professor

**Mobile:** +919435338109

**Email:** subha.deka@gmail.com

Dept. of Forensic Medicine and Toxicology  
Assam Medical College, Dibrugarh, Assam

<sup>2</sup>Professor (**Corresponding Author**)

**Email:** ashokmoondra18@yahoo.com

Dept. of Forensic Medicine and Toxicology  
Kota Medical College, Kota, Rajasthan

<sup>3</sup>Professor and HOD of Forensic Medicine and Toxicology  
Assam Medical College, Dibrugarh, Assam and India

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who were in their basic science stage of medical studies at Assam Medical College, Dibrugarh, Assam in the year 2019 were selected. A validated and pre-texted questionnaire was used to determine knowledge about principles of research. Linear regression models were applied to predict the score of knowledge of the participants. Prior to collection of the data human institutional ethical clearance was taken which include inform consent of the participant.

Before collecting data, a sample workshop was organized for the student of basic science level. The workshop consisted of a lecture, demonstration and interaction of the students that has covered project identification, epidemiological study designs, experimental study designs, science and scientific methods, research ethics, designing questionnaires, research statistics, an introduction to statistical methods. Scientific information, literature search and manuscript preparation were also briefed.

The knowledge and attitudes were assessed using a standard validated questionnaire developed by Vodopivec et al.<sup>4</sup> The data were collected were analyzed using Microsoft Excel.

## RESULTS

In this study, we have assessed undergraduate medical students' knowledge in principles of research methodology and about the factors affecting it. A total of 100 medical students were participated in this research out of 120 students we approached for.

**Table I** shows the knowledge and attitudes of the students. Significant improvement was observed in the mean knowledge score after the workshop, i.e., 82.50% and the

findings are found to be sensitives (p-value .002). However, attitude score after the workshop (63.75%) remains same even after the workshop.

**Table 1** Impact of a workshop on the knowledge and attitudes of UG medical students in principles of research methodology

Traits	Pre-workshop in %	Post-workshop in %	p-value
Knowledge	67.50 + 20.5	82.50 + 18.8	.002
Attitude	63.75 + 14.1	63.75 + 13.6	NS

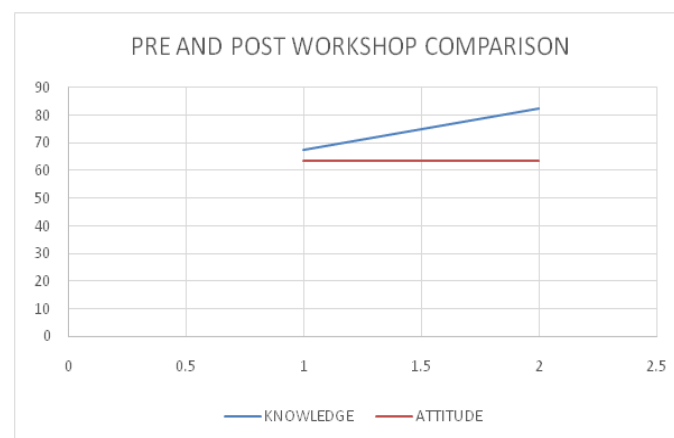


Table 2 summarizes knowledge of the participants in different aspects of research methodology. We observed a good improvement of knowledge of the students after the workshop as shown in **Figure 2**.

**Table 2** Principles of research knowledge score in participants

	Pre-workshop in %		Post-workshop in %		Total
	Yes	No	Yes	No	
Research topic	11	89	40	60	100
Protocol writing	10	90	35	65	100
Primary research	5	95	60	40	100
Secondary research	20	80	70	30	100
Structure of an original article	5	95	90	10	100
Ethical consideration	4	96	95	5	100

## DISCUSSION

The experiences of health research and publication as a medical student has been well demonstrated to be associated with postgraduate research involvement<sup>5</sup> and even among the faculties working in the different medical universities of India as present-day scenario. The present study has also highlighted the increased level of knowledge after attending the workshop.

This study shows medical students have low-to-moderate knowledge about principles of research methodology which

is supported by a study carried out by Windish et al. on understandings of medical residents of biostatistics and interpretation of results, mean correct answer was 41.4%, indicating low-to-moderate knowledge of the medical students in these issues.<sup>6</sup> Similar findings were observed among physicians practicing in an academic medical center,<sup>7</sup> medical students, first year Croatian medical students,<sup>8</sup> Pakistani medical students,<sup>9</sup> and medical students in South East Europe.<sup>10</sup>

The result showed participation in research methodology

workshop independently has improved variance of students' knowledge about principles of research methodology in selection of research topic (40%), protocol writing (35%), concept of primary research (60%), secondary research (70%), structure of an original article (90%) and about the concept of various ethical considerations. This shows the most important factor in students' knowledge on principles of research methodology is attendance in research methodology workshops. In concordance with this finding, Windish et al. found that prior biostatistics training as well as additional advanced degrees contributes to higher mark in understanding biostatistics and interpretation of results.<sup>6</sup> Similarly, Polychronopoulou et al. have shown that prior relevant education in biostatistics is an important predictor of knowledge of biostatistics among European orthodontic postgraduate students.<sup>11</sup>

Considering the fact that some units of medical curriculum are related to health and epidemiology basics, it was assumed that passing these courses would enormously improve students' knowledge on principles of research methodology<sup>12</sup> but our findings suggest that medical course is exclusively important in topics of understanding p-value and secondary studies. However, bewildering factors such as attendance of the students in such workshop or personal interest of students in such interventions may also contribute to the knowledge of students' in principles of research methodology.

A positive attitude of the medical students was not observed in this study even after the workshop regarding their knowledge about research methodology and impact of research workshops. These findings specify that an intensive course may be help to develop the understanding of research methodology and techniques.

**Limitation of the study:** As the sample size is small to draw a definite conclusion. Therefore, a large-scale study is needed to be conducted to confirm these findings.

## CONCLUSION

Brief interventions like workshops, CMEs aimed to enhance the interest and skills of medical students in health research and publications are very much needed as this study has shown a significant improvement on the knowledge regarding principles of health research methodology. However, to improve the attitudes of medical students in principles of research methodology repetitive intervention is required.

The results of this research deliver a useful evidence for policy makers in educating medical students in terms of research and publications.

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**Ethical clearance:** Taken.

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considered for publication elsewhere in any form, except as provided herein. (3) All author(s) have contributed sufficiently in the article to take public responsibility for it and (4) all author(s) have reviewed the final version of the above manuscript and approved it for publication.

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## ORIGINAL RESEARCH PAPER

# Ethnic variation of uric acid level among population in greater Kamrup district

Doungel Nomi<sup>1</sup>, Borah Pollov<sup>2</sup>, Thakuria KD<sup>3</sup>

Received on Dec 21, 2017; editorial approval (revised) on April 11, 2019

### ABSTRACT

**Introduction:** In about 16<sup>th</sup> century gout sounded like a disease out of a novel. Purine leads to high level of uric acid which are deposited in the joints and causing the attack of gout. Gout which is the disease since antiquity is an acute, often recurrent arthritis mediated by the crystallization. Genetic or other influences are important modulator for the serum uric acid level. Many studies have been conducted worldwide to identify the risk factors for hyper uricemia including ethnic, enzymatic and environmental predisposition. **Materials and methods:** The present study was conducted among different communities in Greater Kamrup District. Samples were collected by stratified random sampling technique. Communities selected were Ahom; Adivasi; Bodo, Bengali, Karbi, Manipuri and Marwari. Serum uric acid level in different communities were evaluated and compared. **Results:** Uric acid level of Boro community is higher in comparisons to other communities. Uric acid level of Ahom community is found higher in comparison to Manipuri, Bengali, Adivasi and Marwari. Sex wise uric acid level is high in case of males 5.69 mg/dl, compared to females 4.95mg/dl. **Conclusion:** From the present study, it can be concluded that different communities of Greater Kamrup district depicts different uric acid levels and association with sex. This finding can be associated with dietary habits of different communities. It can be placed in the context of overall health promotion, disease prevention and disease treatment with appropriate attention to nutritional needs in different communities.

**Keywords:** Gout; uric acid; community; purine.

### INTRODUCTION

In about sixteenth century gout sounded like a disease out of a novel.<sup>1</sup> That is probably because this joint disease famously afflicted many luminaries from the past. It has been theorized these historical figures had gout because they had money to

enjoy red meat, sea food and all other food rich in purine.<sup>2</sup> Purine leads to high level of uric which are deposited in the joints and causing the attack of gout. Gout which is the disease since antiquity is an acute, often recurrent arthritis mediated by the crystallization.<sup>3</sup>

Some indigenous people such as Polynesians of Pukapuka in the Cook Island have relatively high serum uric acid level despite on traditional diet that is low in red meat.<sup>4</sup> So, genetic or other influences that are also an important modulation of the serum uric acid level.<sup>5</sup> Many studies have been conducted worldwide to identify the risk factors for hyper uricemia including ethnic, enzymatic and environmental predisposition.<sup>6</sup> Among the acquired factors, reversible life style factor contribute to increased blood uric acid concentration. These factors were suggested to be higher Purine diet, alcohol consumption and obesity.<sup>7</sup>

Objective is to evaluate serum uric acid level in different communities of Greater Kamrup District and compared.

### MATERIALS AND METHODS

The present study was conducted among different communities in Greater Kamrup District. Samples were

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#### Address for correspondence

<sup>1</sup> Associate Professor

**Mobile:** +919864025015

**Email:** nomidoungel@gmail.com

Department of Physiology

Tezpur Medical College, Tezpur, Assam, India

<sup>2</sup> Assistant Professor (**Corresponding Author**)

**Mobile:** +919435030948

**Email:** drpollov@gmail.com

Department of Anaesthesiology

Assam Medical College and Hospital, Dibrugarh, Assam

<sup>3</sup> Assistant Professor

Department of Physiology

Tezpur Medical College, Tezpur, Assam, India

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collected by stratified random sampling technique. Communities selected were Ahom, Adivasi, Bodo, Bengali, Karbi, Manipuri and Marwari. Serum uric acid level in different communities were evaluated and compared.

The study was carried out over a period of 2 years with total number of 280 subjects. 40 subjects from each community consisting of equal numbers of males and females (1:1). They belong from the different community with different occupations and socio-economic status, food habits. They gave informed consent to participate in the study. Subjects are evenly distributed in the age group of 25 years to 70 years.

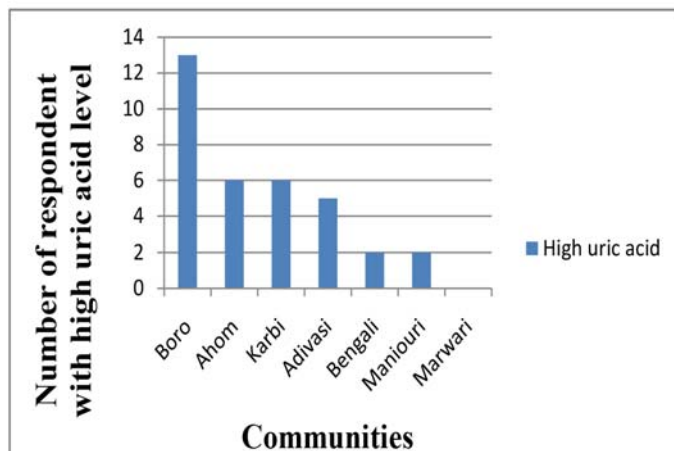
Estimation of serum uric acid was done within 48 hours of collections of the blood samples. Using a calorimeter the biochemical estimations was done. Uricase converts uric acid to allantoin and hydrogen peroxide. The hydrogen peroxide formed further reacts with a phenolic compound and 4 aminoantipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of uric acid present in the sample.

## RESULTS

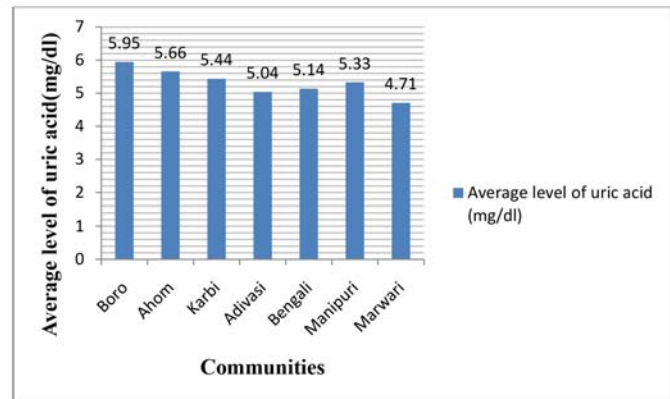
280 patients of Gout were included in this study, out of which 140 were males and 140 were females. Subjects are evenly distributed in the age group of 25 years to 70 years.

**Table 1** High uric acid level among respondents of different community

Community	Total respondent	High uric acid
Boro	40	13
Ahom	40	6
Karbi	40	6
Adivasi	40	5
Bengali	40	2
Manipuri	40	2
Marwari	40	0



**Figure 1** Distribution of high uric acid level among the respondents of different communities



**Figure 2** Average uric acid level of different community

**Figure 2** Depicts uric acid level of Boro community is higher in comparisons to other communities. Uric acid level of Ahom community is found higher in comparison to Manipuri, Bengali, Adivasi and Marwari.

**Table 2** Variation of uric acid level of different community

Source of variation	SS	df	MS	f
Between groups	40.43	6	6.73	5.64
Within group	325.84	273	1.19	
<b>Total</b>	<b>366.27</b>	<b>279</b>		

**Table 2** depicts variation in high uric acid level recorded among the Boro community followed by Ahom, Karbi, Adivasi, Bengali, Manipuri significantly. No cases of high uric acid level were recorded in Marwari community.

**Table 3** Uric acid level of different community vs sex

Community	Male (mg/dl)	Female (mg/dl)	t value (mg/dl)
Boro	6.69	5.22	4.1
Ahom	6.02	5.29	3.09
Karbi	6.09	4.79	3.75
Adivasi	5.43	4.65	2.3
Bengali	5.74	4.53	3.75
Manipuri	4.8	5.85	3.8
Marwari	5.09	4.34	3.57
Overall	5.69	4.95	6.12

Significant at 5% level of significance

**Table 3** depicts Sex wise uric acid level is high in case of males 5.69 mg/dl, compared to females 4.95mg/dl. The average difference of uric acid level of male and female is found to be statistically significant. t - value is 6.12 mg/dl. Incidence of high uric acid level recorded among the Boro community followed by Ahom, Karbi, Adivasi, Bengali, Manipuri significantly. No cases of high uric acid level were recorded in Marwari group.

**Table 3** also illustrated comparative tendency of high uric acid level is more among males as compared to females except among the Manipuri community.

## DISCUSSION

It was observed in categories wise distribution the incidence of high uric acid level was nil in vegetarian categories. In Marwari, out of 40 respondent there is no record of high uric acid. Uric acid in Marwari community is 4.71 mg/dl, much less than other communities. The beneficial effect of dairy proteins relates to the fact that this type of protein cause excretion of urate and contain much lower level of purine. The findings are found to be in consistence with study carried out at different parts of the world.<sup>8,9</sup>

In the non-vegetarian group, often they consumed alcohol daily according to the social customs and religious rituals. It was observed that serum uric acid level in Boro community i.e. 5.95 mg/dl which was comparatively more than the other communities and this finding are similar with studies carried out by different workers.<sup>6,10,11</sup>

Sex wise differences have often been observed and the differences are reported to result from differences in sex hormones. Uric acid level is higher in male is 5.69 mg/dl when compared with female is 4.95 mg.

Sex wise incidence high uric acid was recorded among males in all the communities except the Ahom community. These findings are in consistence with observations of different workers.<sup>4,12,13</sup>

The strength of this study is that it gives some general clue over the altered serum uric acid level in relation to diet. In conclusion it is observed that intake of alcohol and not the purine intake is a strong risk for hyperuricaemia and for the development of gout. And vegetables which are rich in dietary fibres are protective against hyperuricaemia and gout.

## CONCLUSION

Serum uric acid level shows significant variation in different communities like Boro community have high uric acid level in comparison to other communities. Because of their dietary habits. It was seen that there is no significant rise of high uric acid level in Marwari who are strictly vegetarian.

Sex wise high uric acid level is found in males compared to females and the average difference is statistically significant which is similar to all the community except Manipuri.

Serum uric acid may be a marker for the presence of an adverse cardiovascular diseases and it is strongly related to hypertension; hyperlipidemia; diabetes mellitus.

So, from the above study it can be concluded that different communities of Greater Kamrup district depicts different uric acid levels and association with sex. These findings can be associated with dietary habits of different communities. It can be placed in the context of overall health promotion, disease prevention and disease treatment with appropriate attention to nutritional needs in different communities.

A further bio-chemical analysis of blood in persons of different communities, both vegetarian and non-vegetarian dietary habit may help us to know different health problem in our society. Also, a thorough study is needed regarding the quantitative and qualitative evaluation of the constituent of non- vegetarian diet in different community without changing their dietary habit.

So, the above study reflects obvious scope for further work on this observation.

**Conflict of interest:** None declared.

**Ethical clearance:** Taken.

**Source of funding:** None declared.

**Author Disclosure:** The article is original with the author(s) and does not infringe any copyright or violate any other right of any third party.

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## ORIGINAL RESEARCH PAPER

# Role of KIR gene cluster in susceptibility to rheumatoid arthritis

Kakati Pankaj<sup>1</sup>, Misra Dhritiman<sup>2</sup>, Choudhury MK<sup>3</sup>, Talukdar KL<sup>4</sup>, Deka Roonmoni<sup>5</sup>, Baruah Chitralekha<sup>6</sup>

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### ABSTRACT

**Introduction:** Rheumatoid Arthritis (RA) is an autoimmune and chronic inflammatory disease of unknown etiology whose pathogenesis is not fully understood. Small joints in the hands and feet are involved the most. Genetic risk association of RA with HLA-DRB1 gene is the most significant. Women are more affected than men. Natural killer cells and CD28 null T-cells present in synovial membranes of joints of RA patients express Killer cell immunoglobulin-like receptors on its surface. KIR gene cluster has a strong association with autoimmunity as found in various studies. **Objective:** To investigate the role of various genes of KIR gene cluster in the pathogenesis of RA. **Materials and methods:** Blood samples from 80 cases (following ACR/ EULAR criteria-2010) and 80 controls were collected in EDTA vials using standard venipuncture procedure. DNA was extracted from each of the collected blood samples and KIR genotyping was done by molecular techniques using SSP kits. **Results:** The presence of KIR2DS1, KIR2DS3, KIR2DS4, KIR2DS5 and KIR3DL1 genes among RA patients showed risk association. Using standard statistical tools results were validated. **Conclusion:** Some of the KIR genes have risk association with occurrence of RA. Individuals carrying these genes are suspected to be more susceptible to develop RA.

**Keywords:** Pathogenesis; genotyping; risk association; susceptible.

### INTRODUCTION

Rheumatoid Arthritis (RA) is an auto-inflammatory disease whose progression is chronic in nature. It mainly attacks synovial joints but extra-articular involvement can also be seen. Pain, swelling, and stiffness of the joints are the most common signs and symptoms. Most often small joints in the hands and feet are involved, although larger joints may also be involved. Typically joints are affected in a symmetrical pattern; for example, if joints in the right hand are affected,

left hand also tends to be involved. It affects approximately 1% of the population distributed worldwide. The prevalence of RA is higher in women as compared to men.<sup>1</sup> Depending on the age of onset, it reduces the lifespan of the patient by 5-10 years.<sup>2</sup> Pathogenesis of RA has not been fully elucidated till now, even though many researches have been done. As the immune system attacks the body's own tissues and organs, and, due to the presence of autoantibodies like rheumatoid factor (RF) and anti-cyclic citrullinated antibodies (Anti-CCP), it is considered to be an autoimmune disease. As both genetic and environmental factors are involved, it is considered a multifactorial disease. Etiology of the disease comprises of 60% of genetic factors.<sup>3</sup> Variations in human leukocyte antigen (HLA) genes, especially the HLA-DRB1 gene is the most significant genetic risk factors for rheumatoid arthritis. It has been documented that shared epitope (SE) alleles, such as HLA-DRB1\*01 and DRB1\*04, some HLA alleles like HLA-DRB1\*13 and DRB1\*15 are connected to RA susceptibility.<sup>4</sup>

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### Address of correspondence:

<sup>1</sup>Senior Research Fellow and Ph.D. Scholar

**Mobile:** +919401156293

**Email:** pankajkakati1@gmail.com

<sup>2</sup>Ph.D. Research Scholar

**Mobile:** +918761068646

**Email:** dhriti.dhriti@gmail.com

HLA Laboratory, Department of Anatomy

<sup>3</sup>Professor (**Corresponding author**)

Department of Physiology

**Mobile:** +919864034231

**Email:** drmanojchoudhury@gmail.com

<sup>4</sup>Former Professor and Head of Anatomy, Gauhati Medical College & Hospital (GMCH), Guwahati, Assam,

<sup>5</sup>Professor and Head of Anatomy, Tezpur Medical College, Tezpur

<sup>6</sup>Professor of Medicine, GMCH, Assam, India

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The Immune system distinguish the body's own proteins from proteins made by foreign invaders with the help of the proteins produced from HLA genes which is estimated to be 11–37 %.<sup>5</sup> Other genetic risk factors for RA are PTPN22, CD40, CTLA4 and also genes coding elements of NF- $\kappa$ B signaling pathway like TNFAIP3 and TRAF1.<sup>6</sup> Natural killer (NK) cells, which are bone marrow derived large granular lymphocytes, mount early immune responses in an antigen independent manner by direct cytotoxicity.<sup>7</sup> NK cells display Killer cell immunoglobulin-like receptors (KIRs). Located on chromosome 19q13.4, the KIR gene cluster spans about 150–200 kb in the Leukocyte Receptor Complex. By interacting with MHC class I molecules, which are expressed on all cell types, KIRs regulate the killing functions. This interaction allows them to detect virally infected cells or tumor cells that have a characteristic low level of Class I MHC on their surface. The KIRs comprise a multigene family of receptors. KIR gene cluster consists of inhibitory genes, viz., KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1, KIR3DL2, KIR3DL3, KIR2DL4, KIR2DL5; activating genes, viz., KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DS1 and pseudo genes, viz., KIR2DP1 and KIR3DP1.<sup>8</sup> KIR genes like KIR2DL2, KIR2DS2, KIR3DS1 and KIR2DS4 are found to be associated with RA in Iranian, Mexican, Polish, Caucasian, Taiwanese and North Indian populations.<sup>8-13</sup> Studies on the relationship of KIR and RA are inconsistent and contradictory.<sup>14</sup>

In the Northeastern parts of India, only a few studies related to association of genetic factors related to RA, have been done. A recent study found TNF- $\alpha$  –308 variant GA genotype was higher in RA (46.03%) than in control (25%). The presence of TNF- $\alpha$  –308 variant A allele was associated with increased risk of RA susceptibility.<sup>15</sup> Till date, not a single study examining the KIR gene cluster in relation to RA, has been done in this part of India i.e., the Northeastern parts. Hence, the present, study aims to examine the role of various KIR genes in the susceptibility to rheumatoid arthritis among the population of Assam, which is one of the most important states of North East India.

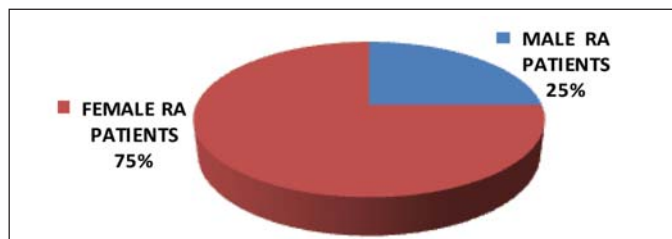
## MATERIALS AND METHODS

The study was conducted in a tertiary care government hospital situated in Guwahati, which is the gateway to Northeast India and where the capital of Assam (Dispur) is situated. This hospital caters to a large number of patients from every region of the state. A total number of 80 cases were taken from the Rheumatology OPD, Department of Medicine, Gauhati Medical College and Hospital, Guwahati, Assam, following the ACR/EULAR criteria (2010), during the period from 2017 to 2019. Four to six milliliters of blood were obtained, from patients diagnosed with RA as per the standard venipuncture procedure and transferred into EDTA vials. Similarly blood samples were also collected from 80 controls who were individuals neither having any history of RA nor any other autoimmune diseases. DNA was extracted from all samples using standard (Manatis, et al) technique.<sup>16</sup> Quality and quantity was checked using Multiscan Go

(Spectrophotometer/Nanodrop). Purity ratio of DNA samples were found to be between 1.8- 2.0 using wavelength 260/280 nm.<sup>17</sup> Concentrations were found to be above 200 ng/ $\mu$ L. PCR amplification of DNA samples of both patients and controls groups for KIR genes were performed using Sequence-Specific Primer (SSP) technique. The amplified products were subsequently loaded in 2% agarose gel submersed in 0.5X Tris buffer in a gel electrophoresis system. After running the electrophoresis for the required period, the 2% agarose gels were documented under gel documentation system. Intercalating agent ethidium bromide was used to tag the DNA in the gels viewed under UV rays using gel documentation system. KIR genes were identified, using appropriate tools, for the KIR genes responsible for inhibitory signals (KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1, KIR3DL2, KIR3DL3, KIR2DL4 and KIR2DL5), activating signals (KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5 and KIR3DS1) and two pseudo genes (KIR2DP1 and KIR3DP1). Results were validated using statistical tools like Fisher's exact test and Chi square test for independence and the findings less than P value- 0.05 were considered as statistically significant.

## RESULTS

After analyzing the data of the study group it has been found that the frequency of female RA patients was higher (**Figure 1**) than male patients (P value<0.0001, OR- 9.0, 95% CI- 4.7450-17.0706). Females were found to be more predominant in terms of disease acquirement.



**Figure 1** Sex distribution among RA patients

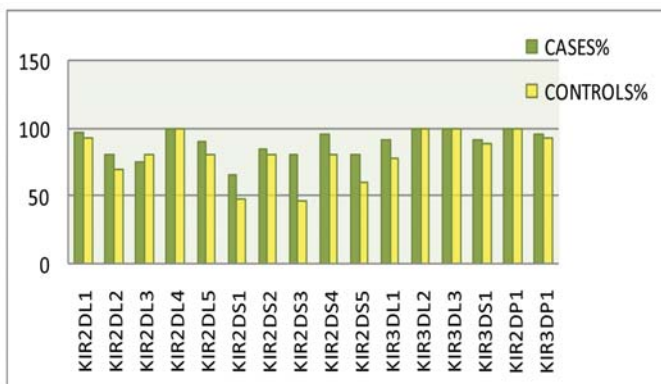
Associations of 16 KIR genes have been portrayed in **Table 1**. Considerable difference in the occurrence of KIR2DS3 gene between the patient and the control group was found during the study. From the univariate analysis comparing RA patient with healthy controls it was found that KIR2DS3 may have a significant role in increasing the susceptibility to RA (P value- < 0.0001, OR- 4.4211, CI- 2.1912 to 8.9200). Apart from that, few other genes from the KIR cluster were found to have risk associations with RA. Those activating genes were KIR2DS1 (P value- 0.0372, OR- 2.0636, 95% CI- 1.0904 to 3.9056), KIR2DS4 (P value- .0072, OR- 4.7500, 95% CI- 1.5115 to 14.9269) and KIR2DS5 (P value- 0.0092, OR- 2.6667, 95% CI- 1.3147 to 5.4091). Moreover, it was found that the incidence of inhibitory gene KIR3DL1 was higher in frequency among the RA patients than the controls in the study population (P value- 0.0446, OR- 2.8141, 95% CI- 1.0965 to 7.2222). The protective functionality of KIR genes in RA as reported in different populations<sup>8-13</sup> was not observed in this study group.

**Table 1** Distribution of the KIR genes in patient and control group

Genes	Patients (n)	Controls (n)	P value	Odds ratio	Confidence interval
KIR2DL1	78	75	0.4426	2.6000	0.4893 to 13.8145
KIR2DL2	64	56	0.1074	1.7143	0.8285 to 3.5473
KIR2DL3	60	64	0.5704	0.7500	0.3558 to 1.5811
KIR2DL4	80	80	-	-	-
KIR2DL5	72	64	0.1198	2.2500	0.9029 to 5.6069
KIR2DS1	53	39	0.0372*	2.0636	1.0904 to 3.9056
KIR2DS2	68	65	0.6734	1.3077	0.5692 to 3.0043
KIR2DS3	64	38	< 0.0001*	4.4211	2.1912 to 8.9200
KIR2DS4	76	64	0.0072*	4.7500	1.5115 to 14.9269
KIR2DS5	64	48	0.0092*	2.6667	1.3147 to 5.4091
KIR3DL1	73	63	0.0446*	2.8141	1.0965 to 7.2222
KIR3DL2	80	80	—	—	—
KIR3DL3	80	80	—	—	—
KIR3DS1	73	71	0.7930	1.3219	0.4671 to 3.7414
KIR2DP1	80	80	—	—	—
KIR3DP1	77	75	0.7194	1.7111	0.3949 to 7.4144

\*Statistically significant.

Distribution of the KIR genes in patient and control group in terms of frequency of occurrences has been illustrated in **Figure 2**.

**Figure 2** Distribution of the KIR genes in patient and control group in terms of frequency of occurrences

## DISCUSSION

RA is an autoimmune disease with immunocomplex mediated hypersensitivity. It drastically involves the synovial joints and has a prevalence of approximately 1%. It affects generally the people of age group 30 to 60 years. Though its etiology is not fully understood still polygenic involvement is suspected to be associated. Whereas KIR has been seen to be associated with various autoimmune diseases and viral complications. The multiallelic diversity of KIR has made it the prime candidate for disease association studies. In this study, an approach has been made to elucidate the relationship between KIR and RA. After investigating the cases and controls drawn from homogenous population of Assam, it has been seen that the incidence of RA is higher in females as compared to



males (P value- < 0.0001, OR- 9.0, 95% CI- 4.7450-17.0706), such findings based on gender variation are also reported in studies conducted on other populations.<sup>1</sup>

Upon univariate analysis of individual KIR genes in the study group, it has been found that KIR2DS1 (P value- 0.0372, OR- 2.0636, 95% CI- 1.0904 to 3.9056), KIR2DS3 (P value- < 0.0001, OR- 4.4211, CI- 2.1912 to 8.9200), KIR2DS4 (P value- 0.0072, OR- 4.7500, 95% CI- 1.5115 to 14.9269), KIR2DS5 (P value- 0.0092, OR- 2.6667, 95% CI- 1.3147 to 5.4091) and KIR3DL1 (P value- 0.0446, OR- 2.8141, 95% CI- 1.0965 to 7.2222) genes have risk associations with RA. Out of these five genes, KIR2DS3 has been found to be highly associated with susceptibility to RA in terms of frequency. A similar finding from Taiwanese population has also been reported where KIR2DS4 was found to be associated with RA.<sup>12</sup> In contrary to our findings, risk association and protective functions of KIR genes are contradictory and inconsistent in different populations. In Mexican population, KIR2DL2 and KIR 2DS2 have risk associations with RA whereas KIR2DL3 seems to confer protection against RA.<sup>9</sup> In Polish population,<sup>10</sup> it has been found that frequencies of KIRs in patients with RA are similar to the frequencies in controls whereas in Iranian population KIR2DL2, KIR2DL5, KIR2DS5 and KIR3DS1 are found to be protective against RA.<sup>8</sup> In North Indian population also KIR association with RA has been studied where they observed KIR3DS1 and KIR2DS2 have risk association however KIR2DL2, KIR2DL3 and KIR3DL1 have protective function.<sup>13</sup>

Another observation was made where KIR3DL1, which is normally classified under inhibitory signaling genes,<sup>8</sup> has been found to be higher in patients than in controls, thus contraindicating its inhibitory role in the population in Assam. Other KIR genes viz., KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5, KIR2DS2, KIR3DL2, KIR3DL3, KIR3DS1, KIR2DP1, KIR3DP1 were found to have similar frequencies in both cases and controls and their relationship with RA could not be statistically proven.

## CONCLUSION

In this study it has been seen that there is an activating role of KIR2DS1, KIR2DS3, KIR2DS4, KIR2DS5 and KIR3DL1 in RA and the individuals with these genes are more susceptible to develop RA. The actual mechanism behind their role in susceptibility is through various cascades of pathways involving the KIR receptors in NK cells, further to validate the findings comparison and confirmation from various independent cohorts is needed. Despite of everything, irreconcilability has been seen in the effort of replicating the result.

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## ORIGINAL RESEARCH PAPER

# Quality of antenatal care and pregnancy outcome in the slums of Guwahati city

Talukdar Rijusmeeta<sup>1</sup>, Madaan Sandeep<sup>2</sup>

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### ABSTRACT

**Background:** The primary aim of antenatal care is to achieve at the end of every pregnancy healthy baby and mother.

**Objective:** To assess the quality of antenatal care (ANC) and its relation to pregnancy outcome.

**Materials and methods:** A community based cross-sectional study was carried out from August 2011-July 2012. Study was conducted in 7 slums in Guwahati city, Assam, selected by systematic random sampling. Total of 400 mothers who had delivered within 1 year were selected randomly and interviewed. Information about socio demographic variables, ANC services and pregnancy outcome were collected. Data were collected in a predesigned, pretested and semi-structured proforma and analyzed using statistical software. **Results:** Majority (81.25%) of mothers were registered for ANC. About 61% mothers had 3 or more ANC out of which 66.25% mothers were registered within 12 weeks of pregnancy. While 81.25% mothers had their BP measured, only 25.75% had 100 or more IFA tablets and 70% had 2 doses of TT, 64.5% had their Hb% estimated, 74.5% were advised on proper rest and nutrition, 75% were aware of danger signs of pregnancy. While 81.25% were informed about institutional delivery, only 55.25% mothers had institutional delivery. Association between IFA consumption by mothers and birth weight of babies was highly significant ( $p < .001$ ). **Conclusion:** Utilization of 3 or more ANC and institutional deliveries were low in the slums. Thus, awareness of benefits of quality ANC must be generated in slums to ensure increased utilization.

**Keywords:** Maternal health; pregnancy care; institutional delivery; birth weight.

### INTRODUCTION

Globally hundreds of women and children are dying due to pregnancy related complications and low income countries are contributing a large percentage.<sup>1</sup> As per WHO, India

contributes 19% of maternal mortality globally.<sup>2</sup> Assam is a priority state with high maternal mortality rates. Infant mortality rate has not improved much and there is a vast difference when compared with high performing states.<sup>3</sup>

Antenatal care is the 'care before birth' to promote the well-being of mother and fetus, and is essential to reduce maternal morbidity and mortality, low-weight births and perinatal mortality.<sup>4,5</sup> However, the content and quality of antenatal care and the availability of effective referral and essential obstetric care are important for antenatal care to be effective.<sup>5</sup> High quality antenatal care is seen as a fundamental right of all women to safeguard their health and that of their infants providing opportunities for risk factor intervention.<sup>5</sup>

The high maternal and infant mortality rate of Assam is an issue of concern and needs to be looked upon. National rural health mission was launched in 2005 for the rural areas, but the poor reside in slums too and whether they have access to and are they utilizing the antenatal services remains unanswered. Programmes and policies have been launched to address the problem but how well are they utilized and how effective are they? The focus of the analysis is on the maternal health care practices, to examine whether and how disadvantaged the pregnant ladies in urban slums are in aspects

### Address for correspondence:

<sup>1</sup> Assistant Professor

Department of Community Medicine

**Mobile:** +918723930817

**Email:** rijusmeeta@gmail.com

<sup>2</sup> Assistant Professor (Corresponding Author)

Department of Anatomy

K.M. Medical College, Mathura, UP.

**Mobile:** +919896542122

**Email:** drsandeepmadaan84@gmail.com

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of maternal care. Considering these facts the study was conducted with the following objective, that is, to assess the quality of antenatal care and to study the association of birth weight and various components of antenatal care.

## MATERIALS AND METHODS

This cross sectional study was undertaken in the slums of Guwahati city, Kamrup Metro district, Assam. The urban slums of Guwahati city is spread over 60 municipal wards covering a population of 1,67,796 with a total of 90 slum pockets encompassing 27,966 households.<sup>6</sup> The slum population under study is a heterogeneous mix of rural-urban migrants, irrespective of religion, language, place of origin and economic status. The study was conducted from August 2011 to July 2012.

**Study population:** The study population includes post natal mothers within 1 year of delivery residing in urban slums of Guwahati city.

**Exclusion criteria:** Women who went to their mother's house for delivery.

**Sample size and sampling design:** According to DLHS 3 (District Level Household Survey), 45.1% of women in Assam avail 3 or more ANC services. Sample size estimated at 5% level of significance with an absolute error of 5% is worked out as follows:

$$n = 4pq/l^2$$

Where, n=sample size

p=prevalence

q=1-p

l=absolute error

n= 400

Out of 90 slums in the city,<sup>6</sup> the slums with less than 100 house-holds were clubbed together and considered as one unit after which the total number of slums came to be 89.

Considering the fact that pregnant women constitute 3% of the total population<sup>7</sup> number of pregnant women per slum is calculated to be 57 approximately. Therefore, to get a sample of 400 mothers 7 slums were visited from a total of 89 slums. The 7 slums were selected by systematic random sampling method using random number table. In each slum, house to house visits were conducted and the lactating mothers were selected randomly to get the desired number of mothers.

**Data collection tools:** Data were collected in a predesigned, pretested and semi-structured proforma

**Data collection technique:** The selected slums were visited and the respondents were carefully briefed about the purpose of the study so as to get full co-operation from them while conducting the study. House to house visits were made till 400 respondents could be found in the selected areas. Interviews were conducted at the house of the respondents. The study being a cross sectional one, only one visit was made to each individual mother.

A pre-designed, pretested, semi-structured proforma was used during the data collection. In the first part of the proforma detailed socio-demographic data were collected. In the next part of the proforma to see the utilisation of the maternal health services, data related to utilisation of antenatal, intranatal, postnatal services and regarding Janani Suraksha Yojana were collected. In the final part of the proforma, information about breast feeding and contraceptive service utilisation was included.

**Data analysis:** Data was structured and analysed using Microsoft excel.

## RESULTS

**Table 1** shows 37.5% of mothers were married at or below 19 years of age and majority of the mothers (86.5%) were in the age group of 20-24 and 25-29 years.

**Table 1** Distribution of mothers by age at marriage and their current age

Age at marriage (in years)	Current age of mother (in years)					Total
	<20	20-24	25-29	30-34	≥35	
<15	6 (1.5)	2 (0.5)	2 (0.5)	-	-	10 (2.5)
15-19	14 (3.5)	70 (17.5)	45 (11.25)	10 (2.5)	1 (0.25)	140 (35)
20-24	-	113 (28.25)	78 (19.5)	-	2 (0.5)	193 (48.25)
25-29	-	-	36 (9)	18 (4.5)	-	54 (13.5)
≥30	-	-	-	3 (0.75)	-	3 (0.75)
Total	20 (5)	185 (46.25)	161 (40.25)	31 (7.75)	3 (0.75)	400 (100)

\*parenthesis in bracket show row wise percentage.

Out of 400 women, 81.25% of mothers were registered for ANC and 18.75% mothers were not registered. As regards number of ante natal checkups and duration of pregnancy at

the time of ANC registration, **table 2** shows that out of 325 mothers, 75% of mothers had more than or equal to three ANC and 6.8% of mothers had only 1 ANC. Majority, 81.54%



of mothers were registered for ANC before 12 weeks of pregnancy and 1.84% mothers were registered for ANC after 28 weeks of pregnancy.

**Table 2** Distribution of mothers by the number of ante natal checkups and duration of pregnancy at the time of ANC registration

No. of ANC	Duration of pregnancy				
	<12 weeks	12–16 weeks	16–28 weeks	>28 weeks	Total
1	6 (1.85)	1 (0.3)	11 (3.38)	4 (1.23)	22 (6.8)
2	33 (10.15)	23 (7.1)	1 (0.3)	2 (0.6)	59 (18.2)
≥3	226 (69.5)	17 (5.23)	1 (0.3)	-	244 (75)
Total	265 (81.54)	41 (12.62)	13 (4)	6 (1.84)	325 (100)

**Table 3** shows that out of the 325 mothers registered for ANC, 100% mothers had their BP and weight measured and also had their abdominal examination done, 92.3% of mothers took TT injection and 91.7% of mothers consumed IFA tablets. Regarding health education & advice received by mothers, 74.5% of mothers were advised on proper nutrition, 75% of mothers were advised on danger signs of pregnancy and

81.25% of mothers were told about the expected date of delivery and about institutional delivery. 80.3% mothers had done ABO grouping and Rh typing, 79.4% of mothers had their blood tested for Hb% and 33.23% of mothers underwent USG during their last pregnancy. Out of the total 400, 48% of deliveries took place in Government hospital, 44.75% were home deliveries and 7.25% deliveries were in a private hospital.

**Table 3** Distribution of mothers as per the categories to assess quality of antenatal care

Variable	Yes	No	Total
Consumption of IFA	298(91.7%)	27 (8.31%)	325 (100%)
Receipt of TT	300 (92.3%)	25 (7.69%)	325 (100%)
BP and Wt taken	325 (100%)	-	325 (100%)
Abdominal examination done	325 (100%)	-	325 (100%)
Advise on proper nutrition	298 (74.5%)	102 (25.5%)	400 (100%)
Advise on danger signs of pregnancy	300 (75%)	100 (25%)	400 (100%)
Told about expected date of delivery	325 (81.25%)	75 (18.75%)	400 (100%)
Advise on institutional delivery	325 (81.25%)	75 (18.75%)	400 (100%)
Hb% done	258 (79.38%)	67 (20.61%)	325 (100%)
ABO and Rh grouping done	261 (80.3%)	64 (19.69%)	325 (100%)
Urine examination done	259 (79.69%)	66 (20.3%)	325 (100%)
Ultrasonography done	108 (33.23%)	217 (66.77%)	325 (100%)
Hospital delivery	221 (55.25%)	179 (44.75%)	400 (100%)

**Table 4** Distribution of mothers by intake of IFA tablets and birth weight of baby

IFA consumption	Birth weight of baby					Weight not taken	Total
		<2000g	(2000-2499)g	≥2500g	Total		
Yes	No.	4	52	113	169 (56.7)	129 (43.3%)	298 (100)
	%	2.4%	30.8%	66.9%	100%		
No	No.	8	42	2	52 (50.98)	50 (49.02)	102 (100)
	%	15.4%	80.8%	3.8%	100%		
Total	No.	12	94	115	221 (55.25)	179 (44.75)	400 (100)
	%	5.4%	42.5%	52%	100%		

## DISCUSSION

The present study was carried out in 89 slums of Guwahati. 400 women who had delivered within last 1 year were interviewed and analysis was done for their ANC service utilization and its subsequent outcome during delivery.

### Comparative analysis:

The findings of different parameters in the present study have been analyzed comparatively with other studies as follows:

The current study shows that significant number of participants (37.5%) got married before 19 years of age. As per Coverage Evaluation Survey Report Assam (2008-09) majority of the mothers surveyed (57.6%) were married at the age of 15-19 years. In AHS (2010-11) it is stated that, percentage of currently married women, aged 20-24 years, married before legal age of 18 years in Kamrup urban is 33.4%. These results corroborate the findings of the current study. To combat the hazards of early marriage and pregnancy awareness should be spread among slum dwellers regarding complications of teenage pregnancies.

Out of 400 women who participated in this study, 325 (81.25%) were registered for ANC. Utilization of individual ANC services was done by all the registered women. Advice on proper nutrition (74.5%), advice on danger signs of pregnancy (75%), and information about the expected date of delivery and about institutional delivery (81.25%), ABO grouping and Rh typing (80.3%), blood test for Hb% (79.4%) and USG during their last pregnancy (33.23%) were the other ANC services provided to them. The findings of the study are almost similar and are in accordance with the findings of CES Assam (2009)<sup>8</sup> and AHS (2010-11).<sup>9</sup> CES Assam (2009) reveals that 67.8% of the total mothers received health education in respect of proper nutrition during pregnancy, 71.9% received delivery advice & 72.5% were told the expected date of delivery. On the other hand, only about 52% of the total mothers were told about signs of pregnancy.

According to AHS (2010-11), percentage of mothers whose blood was examined for Hb estimation for Kamrup district of Assam was 63% and for Kamrup (urban) it was 70.5%. Data of Kamrup district shows, an ultrasound test was performed for 39.8% of pregnancies.

Out of the total 400, 48% of deliveries took place in Government hospital, 44.75% were home deliveries and 7.25% deliveries were in a private hospital. In a study conducted by RRC-NE,<sup>10</sup> showed that 66% of the total deliveries were conducted in govt. hospitals and other govt. facilities like PHC / CHC etc. whereas 7% deliveries were conducted in private health facilities like private hospitals, maternity homes etc.

Findings of the present study regarding utilization of individual ANC services like TT injection (92.3%) and IFA consumption (91.7%) were found to be more than DLHS 3 (2007-2008)<sup>11</sup> which reported consumption of 100 IFA tablets by 36.9% mothers in Assam. P.K. Mony et al (2001)<sup>12</sup> in their study in slums of Vellore town, Southern India found that complete dose of TT was taken by 94.1% mothers.

Out of 400 mothers, 55.25% mothers had their babies weight taken and 44.75% did not have their babies weight taken. Significant statistical association was found between IFA consumption by mothers, ANC check up, advice on proper nutrition and the birth weight of babies. The results of study done by Nisha et al (2014)<sup>13</sup> corroborate the findings of the current study.

## CONCLUSION

The present study shows that there is a need to generate awareness among the slum dwellers to prevent marriage of girls below 18 years of age and to prevent child bearing among young women. This can be done with the help of health workers by conducting regular home visits. They should also motivate the mothers for antenatal checkups. The health workers should inform mothers about the benefits of safe motherhood practices and institutional delivery.

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## ORIGINAL RESEARCH PAPER

# Efficacy of trabeculectomy and manual small incision cataract surgery with posterior chamber intraocular lens implantation

Deka Rita<sup>1</sup>, Das Babi<sup>2</sup>, Nath Anamika<sup>3</sup>

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### ABSTRACT

**Introduction:** Glaucoma co-existing with cataract is frequently encountered in the practice of ophthalmology. The proposed study aims to evaluate the results of Trabeculectomy and manual small incision cataract surgery with posterior chamber intraocular lens implantation (Triple procedure) in cataract with glaucomatous eyes on intraocular pressure control, and visual outcome. **Materials and methods:** The study was conducted on 30 cases admitted in Regional Institute of Ophthalmology, Gauhati Medical College. Cataract cases co-existing with primary open angle glaucoma previously receiving maximally tolerated medication, but with poor control; chronic angle closure glaucoma; intraocular pressure above 22mm of Hg and a visually significant cataract; lens induced glaucoma with field defect in the other eye; pigmentary glaucoma were only included for the study. A thorough ocular examination with slit lamp, tonometry, gonioscopy, ophthalmoscopy, field charting and operative procedure with pre-operative and post-operative care was performed after taking informed consent. **Results:** The mean age of the patients were 55.5 years. Thirty eyes of 30 patients underwent trabeculectomy and SICS with PCIOI. The follow ups were 6 weeks and 6 months. There is a significant decrease of intraocular pressure both in first and second post-operative check-up ( $P < .05$ ). However, there is no significant difference of intraocular pressure between first and second post-operative check-up ( $P > .05$ ). In present study it was found that visual acuity was improved after the surgical procedure in both first and second post-operative check-up as 86.67% and 84.21% respectively. **Discussion:** Triple procedure (Trabeculectomy and manual small incision cataract surgery with posterior chamber intraocular lens implantation) offers better visual rehabilitation, avoids multiple surgeries, economically more feasible and controls intraocular pressure adequately. **Conclusion:** There is significant control of IOP and

improvement in visual acuity in the patients undergoing triple procedure.

**Keywords:** Glaucoma; IOP control; triple procedure; visual outcome.

### INTRODUCTION

The functional severity of the cataract, the amount of glaucomatous optic neuropathy, the level of intraocular pressure control that aid the surgeon in deciding among surgical approaches.<sup>1</sup> There are differing opinions with regard to management of patients with co-existing glaucoma and visually significant cataracts. According to some cataract extraction alone lowers intraocular pressure.<sup>2</sup>

However, nearly all eyes with combined intraocular pressure elevation and cataract will require standard medical treatment for glaucoma within the three to six months after cataract extraction.<sup>3</sup> If surgical intervention for glaucoma is done first, the procedure may hasten the progression of the cataract.<sup>4,5</sup>

There are two potential benefits to the combined surgery: The avoidance of transient increase in intraocular pressure in the post-operative period and long-term control of intraocular pressure with one surgical procedure while removing the visual impairment.<sup>6</sup> That is why, recently the triple procedure has been widely accepted.<sup>7</sup> Although long

### Address of correspondence:

<sup>1</sup>Assistant Professor (**Corresponding author**)

**Mobile:** +919706546372

**Email:** ritadrdeka@gmail.com

<sup>2</sup>Refractionist

**Mobile:** +917002665947

**Email:** dr.babi.das@gmail.com

<sup>3</sup>Post Graduate Trainee

Regional Institute of Ophthalmology

Gauhati Medical College, Guwahati, Assam

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term pressure control was noted to be improved, the ability of combined procedure to protect against transient increase in intraocular pressure was not addressed.<sup>8,9</sup>

To avoid the risk of exposure of the patient twice to the intra and post-operative complications; management of both the conditions at the same operative setting is beneficial to the patient.<sup>10</sup>

## MATERIALS AND METHODS

The present study was conducted on 30 case admitted in Regional Institute of Ophthalmology, Gauhati Medical College over a period of one year.

Inclusion criteria were taken as: (1) Cases having intraocular pressure above 22 mm of Hg and a visually significant cataract. (2) Cases of primary open angle glaucoma previously receiving maximally tolerated medication, but with poor control. (3) Cases of lens induced glaucoma with field defect in the other eye. (4) Cases of chronic simple glaucoma with a field defect in the fellow eye. Cases excluded in this study were: (1) Patients with high myopia. (2) Advanced proliferative diabetic retinopathy of the eye. (3) Uveitis (4) Eyes that had undergone previous filtration surgery. Individual cases were investigated and operated.

A detailed history and clinical examination was done. A examination of eye under slit lamp was done. The examination of the fundus was done with the help of direct and indirect ophthalmoscope and 90 Dioptre lens with slit lamp biomicroscope to evaluate the cupping of optic disc in the operated eye and the fellow eye. Gonioscopy was performed using a three mirror gonio lens. Perimetry was done whenever possible using automated perimeter. Nuclear hardness was evaluated using a slit lamp after dilatation of the pupil to determine a cataract and its grading based on the lens opacity classification system (LOCS-III).

Procedure of trabeculectomy and Manual small incision cataract surgery with posterior chamber intraocular lens implantation was performed by a trained surgeon. All cases received topical steroid antibiotic preparation starting on the next post-operative day onward till the end of 6<sup>th</sup> week. Patients were examined at 6<sup>th</sup> week and 6<sup>th</sup> month to look for control of intraocular pressure and improvement in visual acuity or for any other post-operative complication.

## RESULTS

Statistical analysis for the present study was done using IBM SPSS Version 22. The observations were depicted as below.

**Table 1** Etiological diagnosis of the cases

Diagnosis	No of Eyes	Percentage
Primary open angle glaucoma	18	60%
Chronic angle closure glaucoma	7	23.3%
Lens induced glaucoma with field defect in the other eye	4	13.3%
Pigmentary glaucoma	1	3.3%

**Table 1** shows the etiological diagnosis of cases who underwent trabeculectomy and manual small incision cataract surgery with posterior chamber intraocular lens implantation. The mean age of the patients were 55.5 years (range 31 to 80 years). Majority of the cases are Primary open angle glaucoma (60%) followed by Chronic angle closure glaucoma (23.3%), Lens induced glaucoma with field defect in the other eye (13.3%) and Pigmentary glaucoma (3.3%).

**Table 2** Age wise distribution of the cases

Age in Years	No of Cases	Percentage
31-40	3	10.00%
41-50	14	46.67%
51-60	7	23.33%
61-70	5	16.67%
71-80	1	3.33%

**Table 2** depicts highest number of cases (46.67%) is in the age group of 41- 50 years, followed by 23.33%, 16.67%, 10% & 3.33% in the age group 51-60, 61-70, 31-40 & 71-80 years respectively

**Table 3** Distribution of cases according to Intraocular Pressure(IOP)

Range of IOP (mm of Hg)	No of Eyes	Percentage
21-30	1	3.3%
31-40	16	53.3%
41-50	8	26.7%
51-60	3	10.0%
61-70	2	6.7%

**Table 3** reveals Out of all the cases majority (53.3%) have IOP in the range of 31 - 40 mm of Hg.

**Table 4** Showing mean and  $\pm$ SD of Pre, 1st and 2nd Post-operative values of IOP (mm of Hg)

		Pre-OP	1st Post-Operative	2nd Post-Operative
	Mean	41.33	17.68	16.51
	$\pm$ SD	10.82	7.39	2.76
p value	Between Preoperative and respective column	---	.00*	.00*
	Between 1st and 2nd post operative checkup	---	---	.26**

(p value \* p <.05 = Significant)

The study reveals there is a significant decrease of intraocular pressure both in first and second post-operative check-up ( $P < .05$ ). However, there is no significant difference of intraocular pressure between first and second post-operative check-up ( $P > .05$ ) (**Table 4**).

**Table 5** Response of visual acuity after surgery

	1st Post-Operative	Percentage	2nd Post-Operative	Percentage
Improved	26	86.67%	16	84.21%
Unchanged	2	6.67%	1	5.26%
Worsened	2	6.67%	2	10.53%
Total	30	100.00%	19	100.00%

**Table 5** depicts that visual acuity was improved after the surgical procedure in most of the cases in both first and second post-operative check-up (86.67% and 84.21% respectively). Small number of patients shows unchanged or worsening of visual acuity, which can be attributed to other factors like intra operative complications, cystoids macularoedema etc.

However about one-third of the patients were lost in follow up, which can be attributed to higher percentage of cases showing worsening of visual acuity in second follow up.

## DISCUSSIONS

Glaucoma and cataract are encountered fairly often in patients seeking relief from visual impairment. The visual rehabilitation of patients with glaucoma and cataract appears to be difficult. Extraction of cataractous lens alone rarely relieves glaucoma and hence medical treatment for glaucoma is necessary for life long after lens extraction.<sup>11</sup> The problem can be tackled either by doing filtering surgery first followed by lens extraction at a later date (two stage surgery) or filtering surgery and lens extraction with posterior chamber intraocular lens implantation (triple procedure) at the same time.<sup>12</sup> The advantage of triple procedure is enhanced visual rehabilitation and significant control of intraocular pressure.<sup>13</sup> The avoidance of transient increase in intraocular pressure in the post-operative period and long term control of intraocular pressure with one surgical procedure while removing the visual impairment Hence the procedure is becoming more and more popular nowadays.<sup>14</sup>

From the study we found that there is a significant decrease of intraocular pressure in first and second post operative check-up ( $P<.00$ ).<sup>15</sup> In present study it was seen that in most of the cases visual acuity was improved after the surgical procedure in both first and second post operative check-up.<sup>16</sup>

The present study suggest that triple procedure is a cross-effective and better way to manage co-existing glaucoma with cataract cases.

## CONCLUSION

Glaucoma and cataract are important causes of ocular morbidity in singly or in co-existence. Medical management for controlling intraocular pressure needs live long follow up, while triple procedure is an effective way of controlling intraocular pressure and improvement of vision

simultaneously. Another advantage of triple procedure is that only one time hospitalization and short recovery period is required for the patients suffering from glaucoma with cataract. That is why, recently the triple procedure has been widely accepted.

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## ORIGINAL RESEARCH PAPER

# A clinical study of various diagnostic criteria in evaluation of severity of acute pancreatitis

Agarwala Nishit<sup>1</sup>, Das Smita<sup>2</sup>, Bhuyan K<sup>3</sup>

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## ABSTRACT

**Introduction:** Acute Pancreatitis with rapidly progressive severe inflammatory response is associated with significant morbidity. Early assessment of severity and identification of patients at risk is important for early intensive therapy and timely intervention. The study was taken up to see applicability of various diagnostic criteria in evaluation of severity of acute pancreatitis. **Materials and methods:** The prospective clinical study was carried out amongst the patients admitted with Acute Pancreatitis in a tertiary care Hospital in Assam for a period of one year. Data was collected by predesigned and pretested schedule along with clinical examination and laboratory investigations. Revised Atlanta classification, 2012 of determination of severity of AP was taken as the gold standard and accordingly Ransons, APACHE II, and BISAP score were calculated for severity assessment. The first outcome recorded with the accuracy in determination of severity of Acute Pancreatitis. The final outcome was recorded as per eventuality of the treatment course. Statistical analysis of categorical values were evaluated using Chi square or Fischer exact test. **Results:** The average RANSON score of the severe patients was 3.94. The sensitivity of RANSON'S scoring system was 75% while it had 84.21% specificity in predicting severe acute pancreatitis. The average BISAP score of the severe patients was 2.36. The sensitivity of the BISAP scoring system was 75%, while it had 86.84% specificity in predicting severe acute pancreatitis. The average APACHE II score of the severe patients were 10.34 with sensitivity of 83.34% and specificity of 86.84%. The APACHE II score has demonstrated the highest accuracy for prediction of severe AP (AUC = 0.910, 95% CI: 0.826-0.993). **Conclusions:** APACHE II score was found to be better predictor of disease severity and survivability with good sensitivity and high specificity.

**Keywords:** APACHE II; high specificity; sensitivity.

## INTRODUCTION

Acute Pancreatitis has a highly variable clinical course. In most patients though it takes a self-limiting course 10-20% of patients develop a rapidly progressive severe inflammatory response with significant morbidity. The mortality ranges from 10% to 85%.<sup>1</sup>

Given the wide spectrum of disease seen, the care of the patients with pancreatitis must be highly individualized. Early assessment of severity and identification of patients at risk is important for early intensive therapy and timely intervention for better prognosis. Various scoring systems have been used to assess the severity in Acute Pancreatitis.

The study was to study various diagnostic criteria in evaluation of severity of acute pancreatitis with Ransons, BISAP, APACHE II score and usefulness of the best one in stratification of Severe Acute Pancreatitis (SAP).

## MATERIALS AND METHODS

The prospective study was carried out among the patients admitted in a tertiary care hospital in Assam for a period of one year after obtaining requisite ethics committee clearance. Adult patients with more than age 15 years with clinical

### Address of Correspondence:

<sup>1</sup>Senior Resident

Department of Surgery

**Mobile:** +919435344836

**Email:** mailsurgerygmc@gmail.com

<sup>2</sup>Assistant Professor (**Corresponding Author**)

Department of Clinical Haematology

**Mobile:** +919864068293

**Email:** smitabhuyanghy@gmail.com

<sup>3</sup>Professor

Department of Surgery

Gauhati Medical College and Hospital

Guwahati-781032, Assam, India.

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history of abdominal pain and an increased level of pancreatic enzymes suggestive of acute pancreatitis reporting within 48 hours of onset were included in the study. Patients with other co-morbid conditions like cardiac failure, liver failure, renal failure or any lung pathology, acute on a chronic pancreatitis, recurrent attack of acute pancreatitis and with history of complications like pseudo cyst, pancreatic abscess, etc were excluded from the study. Data was collected by predesigned and pretested schedule along with clinical examination and laboratory investigations. Accordingly Ransons,<sup>2,3</sup> BISAP<sup>4,5</sup> and APACHE II<sup>6,7</sup> score were calculated. The first outcome was recorded with the accuracy in determination of severity of acute pancreatitis. The final outcome was recorded as per eventuality of the treatment course.

Statistical analysis of categorical values were evaluated using Chi square or Fischer exact test. Sensitivity, specificity, positive predictive value and negative predictive value of each scoring system were calculated using the cut-off values for high sensitivity and specificity generated from the Receiver Operator Characteristics (ROC) Curve. A P-value of < 0.005 was considered to be significant. Odds Ratio for each of the scoring systems were calculated based on the Fischer exact test. Comparison of scoring systems in prediction of severe AP, were calculated on the basis of the highest sensitivity and specificity values generated from the Area Under Curve (AUC) generated from the (ROC), using the SPSS version 16.0, in order to determine the accuracy for each of the scoring systems. The following cutoff values were selected for prediction of severe AP: Ranson  $\leq 3$ , APACHE II  $\leq 8$ , BISAP  $\leq 2$ .

RESULTS

The present study comprises of 50 patients suffering from pancreatitis during the study period were taken into consideration. Revised Atlanta classification, 2012 of determination of severity of AP was taken as the gold standard. The severity assessment was done by using Ransons, APACHE II and BISAP scoring systems. The patients were divided into two groups of mild to moderate severity and severe acute pancreatitis. In the present study, age of the patients ranges from 21 to 65 yrs. The mean age of incidence is 43.7 yrs. Out of 50 cases 34 patients were female and 16 patients were male. 38 patients had gall stone disease. Of these 38 patients, 33 patients were female and 5 male patients. 9 patients, all male had history of alcoholism of which one had associated gall stone disease. In 3 patients no cause of acute pancreatitis could be determined and were labeled as idiopathic AP. As per Atlanta Classification 37 Patients (75%) had mild to moderate acute pancreatitis and 13(25%) Patients had severe acute pancreatitis (SAP). Patients with RANSON score more than or equal to 3 were considered severe. In this study 35 patients were considered mild to moderate of which 23 patients were female and 12 patients were male. 15 patients were considered severe out of which 11 were female and 4 were male patients. Biliary

aetiology found in most cases. 26 in mild and 11 in severe category (**Table 1**).

Table 1 Aetiology of acute pancreatitis by Ransons score

Severity	Biliary	Alcohol	Idiopathic
Mild	26	6	3
Severe	11	4	0

The average RANSON score of the severe patients was 3.94. One patient died. Mortality rate for SAP 6.67%. The sensitivity of RANSON’S scoring system was 75% while it had 84.21% specificity in predicting severe acute pancreatitis. The positive predictive value of RANSON’S score was 60% in the study while negative predictive value was 91.43%. There was significant correlation between disease severity and RANSON’S score  $\leq 3$  with P = .0003 (**Figure 1**).

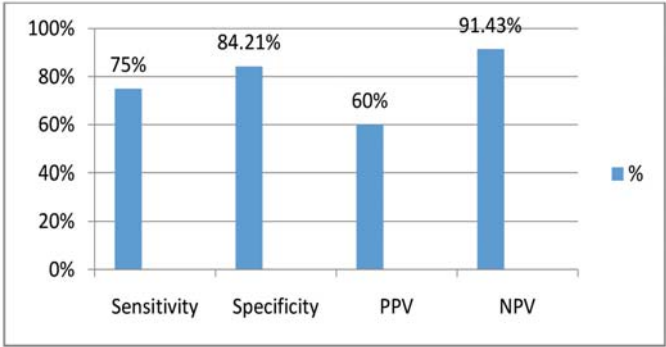


Figure 1 Sensitivity, Specificity, PPV and NPV of Ransons Score in predicting SAP

The average APACHE II score of the patients in the study group was 6.12. Patients with APACHE II score more than or equal to 8 were considered severe.35 patients had mild disease and 15 had severe disease when APACHE II score was used. Out of the 35 mild patients 22 were female and 13 were male. The average APACHE II SCORE of the mild patients was 4.31. Biliary aetiology forms the major part (**Table 2**).

Table 2 Etiology of AP by APACHE II score

Severity	Biliary	Alcohol	Idiopathic
Mild	26	8	1
Severe	11	2	2

The average APACHE II score of the severe patients were 10.34. One patient died with. Mortality rate of 6.67%.The sensitivity of APACHE II scoring system was 83.34%, while it had 86.84% specificity in predicting severe acute pancreatitis. The positive predictive value of APACHE II score was 66.67% in the study while negative predictive value was 94.29%.There was significant correlation between disease

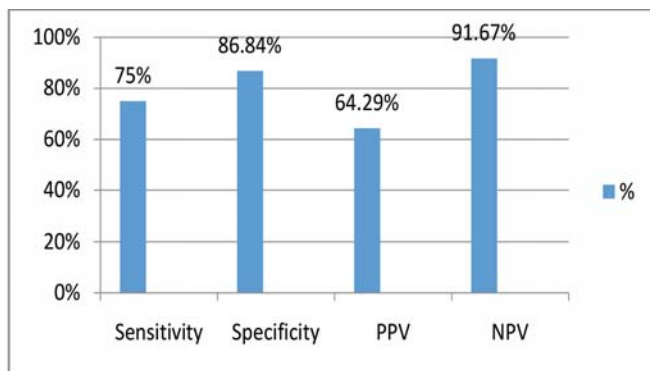
severity and APACHE II score  $\leq 8$  with p value  $< 0.0001$ . Patients with BISAP score more than or equal to 2 were considered severe. 36 patients were considered mild to moderate of which 22 patients were female and 14 patients were male. 14 patients were considered severe out of which 12 were female patients and 2 were male patients. Biliary aetiology constitute major part (**Table 3**)

**Table 3** Etiology of acute pancreatitis by BISAP score

Severity	Biliary	Alcohol	Idiopathic
Mild	26	9	2
Severe	12	1	1

The average BISAP score of the severe patients was 2.36. One patient died showing mortality rate for SAP 7.14%. The sensitivity of the BISAP scoring system was 75%, while it had 86.84% specificity in predicting severe acute pancreatitis. The positive predictive value of BISAP score was 64.29% in the study while negative predictive value was 91.67%.

There was significant correlation between disease severity and BISAP score  $\leq 2$  with p value .0001 (**Figure 3**).



**Figure 3** Sensitivity, Specificity, PPV and NPV of BISAP score in predicting SAP

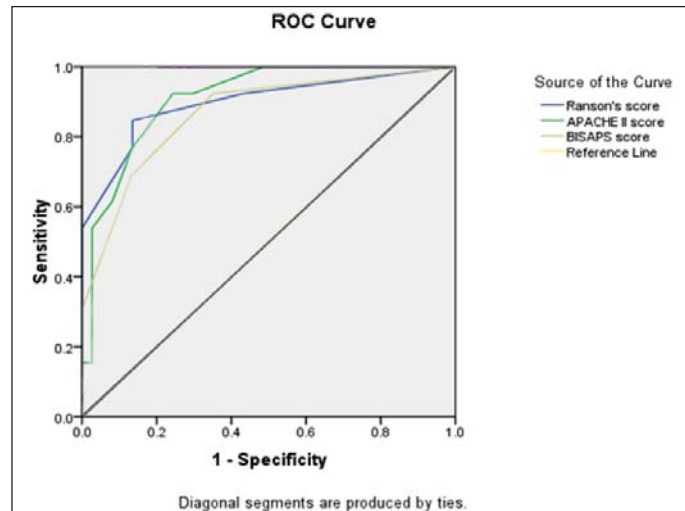
On the secondary outcome of result of treatment of acute pancreatitis the following results were observed as per scoring systems: RANSON Score- 0-3- no mortality  $\geq 3$  -6.67% mortality; APACHE II Score  $<8$ - no mortality  $\geq 8$ - 6.67% mortality; BISAP Score- 0-2 - no mortality  $\geq 2$  -7.14% mortality.

The APACHE II score has the highest sensitivity (83.34%), and PPV and NPV. The specificity and NPV is similar to Ransons and BISAP scoring. There was significant correlation between disease severity and Ransons score  $\leq 3$ , with odds ratio 16.00 and 95% confidence interval 3.325 to 77.003, and p value of 0.0003.

There was significant correlation between disease severity and APACHE II score  $\leq 8$ , with odds ratio 33.00 and 95% confidence interval 5.530 to 196.94, and p value of  $<0.0001$ .

There was significant correlation between disease severity

and BISAP score  $\leq 2$ , with odds ratio 19.800 and 95% confidence interval 3.956 to 99.093, and p value of 0.0001. Receiver-Operating characteristic (ROC) curves for severe AP were calculated for Ransons, APACHE II, BISAP scores, and the predictive accuracy of each scoring system was measured by the area under the ROC curve (AUC) with standard error and 95% confidence interval (CI). A P value of  $< 0.05$  was considered statistically significant. (**Figure 4**)



**Figure 4** ROC: Specificity & Sensitivity of Scoring systems

Taking the revised Atlanta classification (2012) of severe pancreatitis, the sensitivity and specificity of scoring systems were calculated APACHE II score has demonstrated the highest accuracy for prediction of severe AP (AUC = 0.910, 95% CI: 0.826-0.993) (**Table 4**).

**Table 4** Scoring comparisons in assessment of severity

SCORES	SENSITI- VITY	SPECIFI- CITY	PPV	NPV
RANSON'S	75%	84.21%	60%	91.43%
APACHE II	83.34%	86.84%	66.67%	94.29%
BISAP	75%	85.87%	64.29%	91.67%

## DISCUSSION

The present study consists of 50 patients of acute pancreatitis admitted under general surgery and medicine in a tertiary care hospital over period of one year. Three commonly used severity scoring systems has been used to grade the patients namely Ransons, APACHE II and BISAP and an attempt has been made to correlate its most effective application in determination of severity of acute pancreatitis. The age of the patients in the present study ranged from 21-65 years with mean age of 43.7 years. Incidence of disease was highest in the age group 41-50 years (24%). Acute pancreatitis associated with biliary tract calculi showed female

preponderance in the present study. The M:F ratio of acute pancreatitis in this study was 1:2.1. There was male predominance in acute alcoholic pancreatitis (100%) and female predominance was seen in acute biliary pancreatitis (86.8%). Out of 50 cases 34 patients were female and 16 patients were male. Gall stone Pancreatitis was found to be the commonest cause in the study. The overall mortality in this study was found to be 2%.

The sensitivity of RANSON'S scoring system was 75% while it had 84.21% specificity in predicting severe acute pancreatitis. The positive predictive value of RANSON'S score was 60% in the study while negative predictive value was 91.43%. There was significant correlation between disease severity and Ransons score  $\leq 3$ , with odds ratio 16.00 and 95% confidence interval 3.325 to 77.003, and p value of 0.0003.<sup>8,9</sup> The APACHE II scoring system had a sensitivity of 83.3% and specificity of 86.84%. The PPV was 66.67% and NPV was 94.29%. The results of the present study are comparable with the published data.<sup>8,9</sup> The sensitivity of BISAP scoring system was 75%, while it had 86.84% specificity in predicting severe acute pancreatitis. The positive predictive value of BISAP score was 64.29% in the study while negative predictive value was 91.67%. The sensitivity, specificity, and NPV of the present study is comparable with the published data.<sup>6,10</sup> There was significant correlation between disease severity and APACHE II score  $\leq 8$ , with odds ratio 33.00 and 95% confidence interval 5.530 to 196.94, and p value of  $<.0001$ .<sup>11,12</sup> However the present study shows low PPV of 64.29%. There was significant correlation between disease severity and BISAP score  $\leq 2$ , with odds ratio 19.800 and 95% confidence interval 3.956 to 99.093, and p value of 0.0001. In terms of accuracy on applying the ROC curve for the scoring systems the area under curve (AUC) was highest for APACHE II score of 0.910, 95% CI: 0.826-0.993, which is highest among other scoring systems APACHE II score had the highest sensitivity (83.34%) and specificity (86.84%) among other scoring systems for determination of severity of AP. On comparing the accuracy on the ROC curve the APACHE II score has shown the highest area under curve (AUC) of 0.910, with 95% CI: 0.826-0.993.

## CONCLUSIONS

APACHE II score was found to be better predictor of disease severity and survivability with good sensitivity and high specificity. APACHE II score more than 8 was associated with severe disease and mortality. The APACHE II score had the highest sensitivity and specificity among other scoring systems for determination of severity of Acute Pancreatitis.

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published (whole or in part) elsewhere, and is not being considered for publication elsewhere in any form, except as provided herein. (3) All author(s) have contributed sufficiently in the article to take public responsibility for it and (4) all author(s) have reviewed the final version of the above manuscript and approved it for publication.

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## ORIGINAL RESEARCH PAPER

# Assessment of awareness, knowledge, attitude and practice regarding organ donation among medical teachers and post-graduate

Nayak Manjit<sup>1</sup>, Khubchandani HT<sup>2</sup>, Patani Kalpesh<sup>3</sup>, Dewangan Tikendra<sup>4</sup>

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### ABSTRACT

**Introduction:** Organ donation deals with the surgery which includes harvesting the organ and transplants them into end stage organ disease patient which on progression required organ transplantation surgeries. Organ donation rate in India is only 0.26 per million.<sup>1</sup> Absence of consciousness about the requirement of organ donation and the unfamiliarity among medical fraternity regarding its significance knowledge and legal issues create the huge splintering for end stage organ disease Patient. The objective of this study is to assess the awareness, knowledge, attitude and practice regarding organ donation among the Medical Teachers, & students perusing Post-Graduation. **Materials and methods:** Study was conducted among 100 subjects, where 50 Medical Teachers & 50 students pursuing Post-Graduation have participated. Questionnaires are distributed in order to assess their awareness, knowledge, attitude and practice regarding organ donation among the Medical Teachers, & students perusing Post-Graduation. Collected Data was analysed using Microsoft Excel program. **Results:** Total 100 subjects participated in this study, among this 50 are Medical Teachers & 50 are student pursuing post-graduation. Only 33% have gone through the provisions of Transplantation of human organ & tissue act, 1994, although 68% among them have motivated the patient's relative for the organ donation. **Conclusion:** Requirement for organ donation have been showing tremendous upsurge trends as there are increased number of patients diagnosed with end stage organ disease. On the other side lack of awareness, knowledge, attitude and practice regarding organ donation shall hamper the current scenario for upgradation of health status among end stage organ disease patient.

**Keywords:** organ transplantation, end stage organ disease, brainstem death, Transplantation of Human Organs (THO) Act

### INTRODUCTION

Human organ and tissue transplantation were started in India

in 1962. In the beginning, the organ transplant was unregulated, and organ trafficking was extensive. The act governing the transplantation was passed in 1994. This has been consequently modified in 2011, and new rules came into force in 2014. Many of the students as well as practicing physicians are not aware of the act as it is generally not a part of the syllabus. Organ transplantation is considered as the greatest advances of recent science that deals with organ retrieval, harvesting, and transplantation for end stage organ diseases for therapeutic purpose & prevents their commercial dealings. The act was initiated at the request of Maharashtra, Himachal Pradesh, and Goa (who therefore adopted it by default) and was subsequently adopted by all states except Andhra Pradesh and Jammu and Kashmir. Despite a regulatory framework, cases of commercial dealings in human organs were reported in the media. An amendment to the act was proposed by the states of Goa, Himachal Pradesh, and West Bengal in 2009 to address inadequacies in the efficacy, relevance, and impact of the act. The amendment to the act was passed by the parliament in 2011, and the rules were notified in 2014. The same is adopted by the proposing states and union territories by default and may be adopted by other states by passing a resolution. There are some differences between act of 1995 and subsequent rules passed in 2014.<sup>2-4</sup>

### Address for correspondence:

<sup>1</sup>Tutor (Corresponding author)

**Mobile:** +919998227871

**Email:** manjit8889@gmail.com

<sup>2</sup>Associate professor

**Mobile:** +919427713663

**Email:** h\_khub@yahoo.co.in

<sup>3,4</sup><sup>rd</sup> year resident doctor

Department of Forensic Medicine & Toxicology, B.J Medical college, Ahmedabad.

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The total number of road accident fatalities reported in 2013 in India was 1,37,572, contributing to almost 1.1% of the world's total deaths. In nearly 40 to 50% of road accident fatalities, the cause of death has been head injury.<sup>5</sup> These victims of head injury from road traffic accidents alone, are in enough numbers to meet the demand of potential donors of organs in the country. The total organ donation shortage of the country can be met with if even 5 to 10% of these persons involved in fatal accidents serve as organ donors. This is, however, an utopian situation and there are a number of barriers and challenges that are at play in achieving this goal of completely meeting the demands for organ donation. There is a great mismatch between the number of potential donors and actual cadaveric donors. Even in the case of individuals who have given consent for donation after death, the influences of the familial members might change the actual decision. Lack of awareness, superstitions, delay in funeral, lack of agreement between family members, fear of social criticism and dissatisfaction with the hospital staff might all influence their decision. It is here that the involvement of other stakeholders, non-governmental organizations and religious leaders would help in imparting awareness and knowledge and in changing the attitude of the general public towards deceased organ donation. Ultimately, the National Organ and Tissue Transplant Organization (NOTTO) needs to be strengthened so that it may play a central role in coordinating the activities of deceased organ donation.<sup>6</sup>

Clinical guidelines for determining brain death are not consistently validated by the presence of irreversible brain stem ischemic injury or necrosis at autopsy. They do not, therefore, completely exclude the reversible loss of integrated neurological functions in those certified as potential donors. Several critical brain structures remain viable and continue

integrated neurological functioning after clinically determined brain (stem) death occurs. These include electroencephalogram activity, and hypothalamic functions. A recent review of the clinical literature<sup>7</sup> found evidence that suggested preservation of the hypothalamic function in a substantial proportion of patients declared dead by the neurologic criteria. Approximately half of the patients reported in the literature showed evidence suggesting the presence of osmoregulation via the regulated secretion of vasopressin (anti- diuretic hormone). A substantial proportion of patients were also secreting hypophysiotropic hormones originating in the hypothalamus. Patients with preserved cortical electrical activity or intracranial blood flow are considered to be dead in countries that utilize a brain stem criteria, but not dead in those where a whole-brain criteria is applied. Brain stem death has a lower burden of proof than whole-brain death.<sup>8</sup>

This article aims to report on awareness, knowledge, attitude and practice regarding organ donation among the medical teachers and students pursuing post-graduation at BJ Medical College, Civil Hospital Ahmedabad.

## MATERIALS AND METHODS

Randomly, a total of 100 participants are chosen for this study among whom 50 are medical teachers and 50 are students pursuing post-graduation. Multiple choice questionnaire was distributed among them to respond. Answers were framed to assess the awareness, knowledge, attitude and practice. The clearance of Human Institutional Ethical Committee was obtained. Data thus collected were analyzed by Microsoft Excel Software.

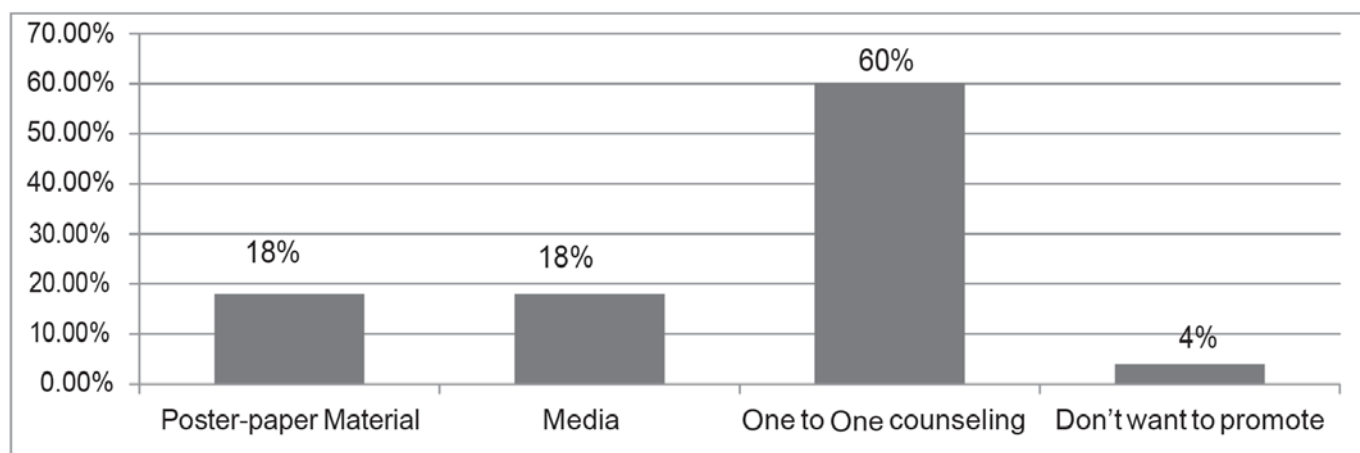
## RESULTS

Collected data has been presented in tabulated form as shown in **Table 1**.

**Table 1** Tabulated form of variables

S.No.	Question	Response	Total percentage	Percentage among Medical Teachers	Percentage among student pursuing post-graduation
1	Have you ever gone through provisions of Transplantation of human organ & tissue act,1994 ?	Yes	33.00%	22.00%	11.00%
		No	47.00%	17.00%	30.00%
		Some extent	14.00%	10.00%	4.00%
		Not Exactly	6.00%	1.00%	5.00%
2	Which of the following does not come under human organ transplantation & tissue act,1994?	Hair	18.00%	10.00%	8.00%
		Skin	Nil	Nil	Nil
		Blood	14.00%	10.00%	4.00%
		All Of the above	68.00%	40.00%	28.00%
3	According to organ transplantation act of 1994, what is the punishment for the doctor if found guilty of removing organs without authority?	5 year & Rs 10,000 fine	24.00%	10.00%	14.00%
		2 Year & Rs 10,000 Fine	11.00%	10.00%	1.00%
		10 Year & Rs 10,000 Fine	24.00%	15.00%	9.00%

		10 Year & Fine up to Rs. 20 lakhs	41.00%	30.00%	11.00%
4	Which disease affected donor cannot donate organ?	HIV	11.00%	9.00%	2.00%
		Hepatitis B	Nil	Nil	Nil
		Diabetes	Nil	Nil	Nil
		All Of the above	89.00%	45.00%	44.00%
5	Have you ever motivated the patient's relative for organ donation during your practice?	Yes	68.00%	30.00%	38.00%
		No	32.00%	20.00%	12.00%
6	Is there any brain death declaration committee existing in your institute?	Yes	31.00%	25.00%	6.00%
		No	15.00%	10.00%	5.00%
		May be	14.00%	9.00%	5.00%
		Don't know	40.00%	10.00%	20.00%
7	Which of the following criteria is not included for declaration of brain death?	Apnea Test	33.00%	20.00%	13.00%
		Brain stem reflex	18.00%	12.00%	6.00%
		EEG	18.00%	14.00%	4.00%
		All Of the above	31.00%	20.00%	11.00%
8	If you find any brain death patient and relative insist for organ donation, then whom will you contact first?	Medical superintendent	13.00%	9.00%	4.00%
		IKD	24.00%	14.00%	10.00%
		Don't know	53.00%	20.00%	33.00%
		Treating doctor	4.00%	1.00%	3.00%
		Forensic medicine Department	6.00%	1.00%	5.00%
9	How you promote & motivate the people for organ donation?	Poster-paper Material	18.00%	10.00%	8.00%
		Media	18.00%	10.00%	8.00%
		one to one counselling	60.00%	42.00%	28.00%
		Don't want to promote	4.00%	1.00%	3.00%
10	What is the age limit for donating kidney?	18-55 year	69.00%	60.00%	9.00%
		No age limit	18.00%	6.00%	12.00%
		Above 18 year	7.00%	3.00%	4.00%
		Below 18 year	6.00%	1.00%	5.00%
11	Are you willing to donate your own organ?	Yes	55.00%	30.00%	25.00%
		No			
		will think about it	40.00%	31.00%	9.00%
		My religion not permit	3.00%	1.00%	2.00%
12	Which live relative can donate liver to the recipient?	Wife	17.00%	11.00%	7.00%
		Cousin brother	1.00%	0.00%	1.00%
		Sister in Law	5.00%	2.00%	3.00%
		All of the above	77.00%	65.00%	12.00%



**Figure 1** Preferred survey type by subjects involved in this study regarding the promotion & motivation of the people for organ donation

## DISCUSSION

In the clause of awareness and knowledge foundation, only 33% have gone through the provisions of Transplantation of Human Organ and Tissue Act, 1994. Among them 22% are medical teachers and 11% are students pursuing post-graduation. Among them only 14% have gone through some extent of the provisions while 6% have not gone through the provisions. However continuous medical education and healthcare professional awareness camp can boost up this number. Looking on the attitude foundation major factor is the motivation for organ donation. 32% of the subjects never motivated the end stage organ disease affected patient's relative. Even 20% of medical teacher have never motivated the relative. In this clause awareness about the legislative procedure and intention for welfare of the society is needed. By motivation definitely there will be increase in the number of organ donation practice. Only 31% of the subjects know that the brain death declaration committee exists in the institute. Also the awareness and knowledge about the proper legislative procedure is required to increase the organ donation percentage in brain death deceased.

India enacted a law in 1994 to legalize the recognition of brain-stem death. Maharashtra has recently mandated the notification of brain-dead cases.<sup>9</sup> The Government Resolution underlines the responsibilities of hospitals registered under the Transplantation of Human Organs (THO) Act 1994, that is, they are authorized transplant centres. As a large number of brain-deaths occur in hospitals not authorized to do transplants, the appropriate authority (Director of Health Services) has registered all hospitals in the state that have an operation theatre and ICU as Non-Transplant Organ Retrieval Centres (NTORCs).<sup>10</sup> These hospitals are permitted to certify brain- death as per the prescribed procedure and then conduct organ retrieval for therapeutic purposes; however, they are not permitted to perform an actual transplantation. Thus, it is mandatory now for all NTORCs and authorized transplant centres in the state to certify and notify the brain-death cases to the Zonal Transplantation Co-ordination committee. This

is a strong step to streamline the procedure for cadaveric organ retrieval and transplantation. In India, there is no legal definition of death. Section 46 of the Indian Penal Code states, "the word 'death', denotes death of a human being unless the contrary appears from the context". India follows the UK practice and considers death as equivalent to brain stem death. Medically and legally, the patient is dead, if brain stem death (brain death is used as a synonym for the latter) has been certified. The doctors involved in the diagnosis should in no way be connected with the transplant surgeries concerning the 'brain-stem dead' cadavers. The certification should be done on the laid out forms (Form No. 8) as per the Transplantation of Human Organs Act. The declaration of brain death must be recorded in the medical notes with the date and time. The legal time of death is the time at which the second prescribed clinical tests are carried out. Comprehensive reviews of brain stem death and brain death from an Indian perspective have also been documented.<sup>11-13</sup>

Currently, America has around 1,20,000 people waitlisted for organs. This is something private players in the US have also tried to raise awareness about. For instance, in 2013, Facebook allowed users to add their "donor status" to their profiles which lead to a spike in registrations. More recently, Apple offered its users in the US to sign up as donors through their iPhones as a part of their iOS 10 software update. Brazil tried to implement the presumed consent model for organ donation in 1997 only to repeal the law 8 years later. The initiative faced heavy criticism and was widely distrusted by the general public who feared that their organs would be removed before they were declared clinically dead. These protests forced Brazil to go back to the opt-in system and its current donation rate is 16 per one million people.

## CONCLUSION

By research and assessment among the medical teachers and students pursuing post-graduation, we found out that there is gap between the participant and society related to knowledge, attitude and practice related to organ donation.

Continuous Medical education & training including awareness can bring the change in the practice of organ donation, their associating legislative procedure for the well being of the patient suffering from end stage organ disease. Motivation and promotion throughout the community by the healthcare providers is essential in the current scenario of organ donation practice. Newer healthcare promotion technology instruments on social media can bolster the awareness and legal knowledge among the medical fraternity and society.

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**Ethical clearance:** Taken.

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**Contribution of authors:** We declare that this work was done by the author(s) in this article and all liabilities pertaining to claim relating to the content of this article will be borne by the authors. The study was conceived and designed by Dr Manjit Nayak; data collection and analysis by Dr Manjit Nayak, Dr H.T Khubchandani, Dr. Kalpesh Patani and Dr. Tikendra Dewangan.

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## ORIGINAL RESEARCH PAPER

# Zinc and ferritin in haemoglobinopathies an observational study

Teli AB<sup>1</sup>, Sarma Nibedita<sup>2</sup>, Baruah Aditi<sup>3</sup>

Received on April 28, 2019; editorial approval on June 10, 2019

### ABSTRACT

**Introduction:** It has been estimated that with a population of 1000 million at the millennium year 2000 and a birth rate of 25 per thousand, there would be about 45 million carriers and about 15,000 infants born each year with haemoglobinopathies in India. The present study is taken up with special emphasis to paediatric patients with thalassemia major and sickle cell anaemia. **Objective:** To measure serum zinc and ferritin levels in paediatric thalassemia major and sickle cell anemia patients. **Materials and methods:** Serum zinc estimated by colorimetric method and ferritin by immunoradiometric method. **Result:** Mean  $\pm$  S.D. of zinc in thalassemia major found to be lower than sickle cell disease with zinc being in lower side of normal range in sickle cell anemia cases suggesting hypozincemia in both groups whereas Mean  $\pm$  S.D. of ferritin found to be higher in both the groups indicating iron overload in both the groups. **Conclusion:** Decreased zinc level and increased ferritin level found in the study may be caused by disease itself or may be consequence of repeated transfusion which has to be ruled out by further study in larger patient groups and meanwhile nutritional supplement of zinc and iron chelation therapy must be mandatory in these group of patients.

**Keywords:** Transfusion overload; nutritional supplement; chelation; Assam.

### INTRODUCTION

Hemoglobinopathies are a group of inherited disorders characterized by abnormal structure or production of haemoglobin caused by gene mutations. While iron deficiency is the most common cause of acquired anemia, haemoglobinopathies have emerged as the most common cause of hereditary anemia. The carrier frequency of haemoglobinopathy varies from 3 to 17% in different population groups of India.<sup>1</sup>

The cumulative gene frequency of the three most predominant abnormal haemoglobins, i.e., sickle cell, haemoglobin D and haemoglobin E has been estimated to be 5.35% in India.<sup>2</sup> Thus, there is a tremendous amount of burden of haemoglobinopathies in India.

Historically, the majority of children who were carriers of these diseases died during their first 10 years of life from complications. However, recent important advances have extended the average life of patients and significantly improved their quality of life. Improved understanding of the etiology and mechanisms of anemia, earlier diagnosis, new therapeutic approaches and better management of transfusion related iron overload have dramatically improved the clinical picture.<sup>3</sup>

Trace elements play an important role in many biological systems because they act as activators or inhibitors, hence competing with other elements and protein for binding site, influences the permeability of membrane.<sup>4</sup> Iron and zinc are essential trace elements in human body and are often altered in patients with thalassaemia and sickle cell anaemia in which

### Address for correspondence:

<sup>1</sup>Associate Professor

**Mobile:** +919435390433

**Email:** dr.anjub.t@gmail.com

Dept. of Biochemistry

Jorhat Medical College And Hospital, Jorhat, Assam

<sup>2</sup>Consultant Biochemist (**Corresponding Author**)

**Mobile:** +917478950641

**Email:** nibedita.amc@gmail.com

Ashadeep Diagnostic Centre

Tarapur Central Hospital

P.O. Malancha, District: Murshidabad, West Bengal

<sup>3</sup>Associate Professor,

Dept. of Pediatrics, Assam Medical College And Hospital,  
Dibrugarh, Assam

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they may play a role in pathogenesis. The alteration of these elements combined with excess amounts of haemoglobin subunits enhance the generation of oxygen radicals after a chain of reactions leading to early death of the red cells and haemolysis.<sup>5</sup> Iron overload is an unavoidable complication suffered by thalassemia major patients as a consequence of excessive number of blood transfusions. It is so common that it has been referred to as a “second disease” during treatment of first.<sup>6</sup>

Iron overload from chronic transfusion therapy can be extremely toxic. Excess transfusional iron is deposited in the liver, heart, and other organs as free iron, which can cause organ dysfunction and damage over time. Zinc (Zn) is an essential nutrient for all forms of life and its importance lies in the fact that many body functions are linked to zinc containing enzymes.<sup>7</sup>

Zn has an indispensable role in human health and diseases. It has been insufficiently recognised by a number of experts as an important public health issue, especially in developing countries. It is the most abundant intracellular metal ion found in cytosol, vesicles, organelles and in the nucleus.<sup>8</sup> However, even a small deficiency is a disaster to human health, so as such the number of biological functions, health implications and pharmacological targets that are emerging for zinc has evoked further interest regarding its status in human health and nutrition.<sup>9</sup>

The present study aims to measure serum zinc and ferritin and their co-relation in patients with haemoglobinopathies.

## MATERIALS AND METHODS

100 cases diagnosed as haemoglobinopathies, including both outdoor patients and patients admitted in the Department of Paediatrics of Assam Medical College and Hospital, were taken for the study. The study group was further subdivided into two groups one as thalassemia and other as sickle cell disease. Thalassemic group was again subdivided into homozygous thalassemia major, heterozygous E-thalassemia and S-thalassemia. Similarly sickle cell disease group was also subdivided into homozygous sickle cell disease and heterozygous E-sickle cell disease.

**Inclusion criteria:** 100 cases, both male and female, in the age group 1-16 years were included on the basis of detailed history and clinical diagnosis. Newly diagnosed patients of haemoglobinopathies (thalassemia and sickle cell anaemia) without transfusion and those coming for follow up and transfusion therapy. Diagnosed patients of haemoglobinopathies without having any oral medication that contain iron, zinc preparation for at least 2 months duration.

**Exclusion criteria:** Haemoglobinopathies associated with other haemolytic disorder (e.g. G-6PD deficiency), severe malnutrition, repeated respiratory infection, thalassemia minor and intermedia.

**Laboratory investigations:**

- R/E Blood, Complete haemogram

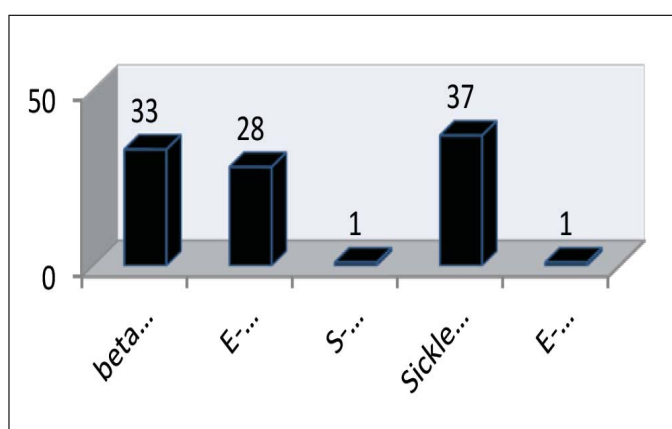
- Hb typing by cation exchange high performance liquid chromatography (BIO-RAD D-10)<sup>10</sup>
- Sickling test using Na metabisulphite method (if necessary)
- Serum Zinc measured by colorimetric method (in semiautoanalyzer, microlab 300 MERK)<sup>11,12</sup>
- Serum Ferritin measured by MAG-16 kit, which is an immunoradiometric assay kit.<sup>13</sup>

Students ‘t’ test was used for comparison of quantitative variables. Co-relation between serum zinc and ferritin were evaluated using Pearson Co-relation Co-efficient. All tests were considered statistically significant if the p-value was <0.05.

To see the correlation between two variables co-efficient of correlation (r) is applied.

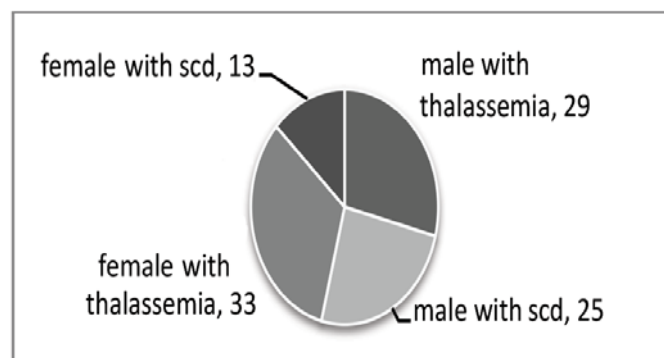
All statistical analysis were done in Microsoft Excel and Graphpad instat.

## RESULT



**Figure 1** Distribution of cases according to HPLC result

It is seen from **Figure 1** that homozygous beta thalassemia, heterozygous E-thalassemia and homozygous sickle cell anemia cases are more prevalent in this study.



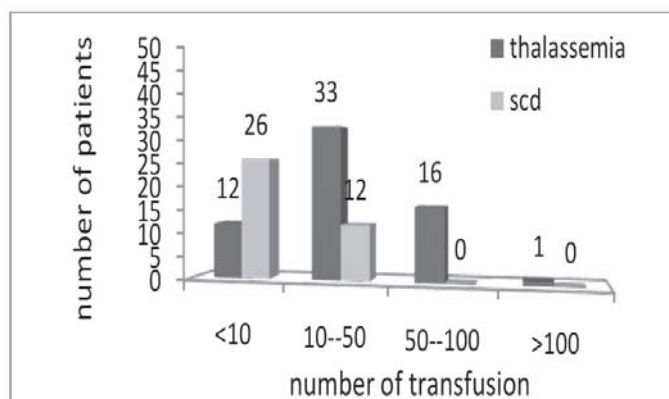
**Figure 2** Distribution of cases according to gender

As seen in **Figure 2** majority of the thalassemic patients in the present study were female (53.23%) whereas majority of the sickle cell disease patients were male (65.78%).

**Table 1** Patients based on level of serum ferritin (ng/ml)

STUDY GROUP	< 100		100-500		500-1000		>1000	
	n	%	n	%	n	%	n	%
THALASSEMIA	1	1.61	6	9.68	20	32.26	35	56.45
SICKLE CELL ANEMIA	2	5.26	13	34.22	18	47.37	5	13.15

as seen in **Table 1** ferritin levels are more than 1000 in majority of thalassemia cases whereas it is within 1000 in sickle cell anemia cases. It may be due to variation in number of transfusion in both groups.

**Figure 3** Distribution of cases according to number of transfusion received

As seen in **Figure 3** maximum 33 number of thalassemic patients (i.e.53.22%) have received transfusion 10-50 times and in sickle cell disease maximum 26 number of patients (i.e.68.42%) have received transfusion <10 times. Mean number of transfusion in thalassemia and sickle cell disease patients are found to be  $34.20 \pm 29.10$  and  $6.5 \pm 5.7$  respectively.

**Table 2** Comparison of mean serum zinc ( $\mu\text{g/dl}$ ) level between the study groups

STUDY GROUP	ZINC (MEAN $\pm$ S.D.)	p value
THALASSEMIA	$71.85 \pm 16.40$	0.98
SCD	$72.17 \pm 14.97$	

In **Table 2** it is observed that mean serum zinc level in thalassemic patients is lower in comparison to sickle cell disease patients but the difference is statistically not significant.

**Table 3** Mean serum ferritin (ng/ml) level between the study groups

Study Group	Ferritin (mean $\pm$ S.D.)	p value
THALASSEMIA	$1130.53 \pm 457.60$	<0.0001
SCD	$620.92 \pm 359.76$	

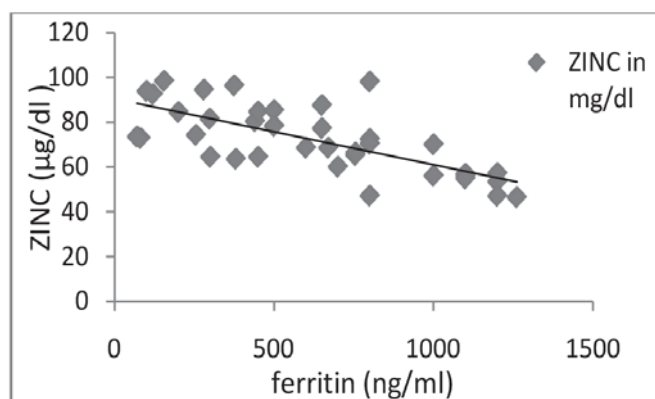
In **Table 3** it is observed that the mean serum ferritin (ng/ml) level in thalassemic patients is higher than the sickle cell disease patients and the result is statistically highly significant.

**Table 4** Co-relation of serum zinc with ferritin in thalassemia major patients

Parameter	Correlation co-efficient (r)	p value
Zn vs Ferritin	-0.39	<0.0001*

\*statistically significant

**Table 4** shows zinc has negative co-relation with ferritin in thalassemia cases and it is statistically highly significant.

**Figure 4** Co-relation of zinc with ferritin in sickle cell anemia patients

**Figure 4** shows zinc has negative co relation with ferritin in sickle cell anemia cases and it is statistically highly significant

## DISCUSSION

In the present study, mean  $\pm$  S.D. of serum zinc level in thalassemia patients is found to be  $71.85 \pm 16.40 \mu\text{g/dl}$  and that of sickle cell disease found to be  $72.17 \pm 14.97 \mu\text{g/dl}$ . The mean level of zinc is within normal reference interval but on lower side in both the study groups indicating hypozincemia. In thalassemia patients zinc level is numerically found to be less than sickle cell disease patients, but this difference is statistically not significant ( $p=0.98$ ).

Zahraa MA Naji in his study on “Serum Trace Elements (Zinc, Copper and Magnesium) in Iraqi Patients with Thalassemia Major Receiving Desferrioxamine and its Relation with Growth State” found that patients with thalassemia major showed lower levels of serum zinc as compared to that of control subjects ( $p<0.05$ ), which indicates that most of patients had hypozincemia; he concluded this may be related to dietary

insufficiency of zinc in those patients in addition to the effects of disease and desferrioxamine administration without dose adjustment for each patient.

Mahyar et al., found that the mean concentrations of serum zinc was  $67.35 \pm 20.38$   $\mu\text{g/dl}$ . Their study revealed that hypozincemia is common in thalassemic patients.

Although many studies revealed low serum zinc in thalassemia patients at least one study by Mehdi-zadeh M et al revealed significantly higher serum zinc in the thalassemic group with no significant correlation between serum zinc level and serum ferritin level, so indicates zinc deficiency in thalassemic patients, who are on regular blood transfusion is rare.

Bot Y.S et al<sup>14</sup> study on "Analyses of Cu and Zn in serum of sickle cell disease patients in Jos" found that a significantly low zinc concentration was obtained from the general comparison of sickle cell disease patients with control subjects.

Zemel et al., 2002; Singhi et al., 2003 in their study found that the biochemical evidence for zinc deficiency in patients with SCD includes low zinc concentrations in plasma, erythrocytes, hair lymphocytes and granulocytes.

In another report by Parad, et al. (1975), low activities of zinc dependent enzymes such as carbonic anhydrase, alkaline phosphate and thymidine kinase found in SCD patients.

A higher than normal activity of plasma ribonuclease in patients with SCD is also seen because zinc is known to inhibit the activities of this enzyme (Parad et al., 1975).

Zinc deficiency can also be the result of the adverse effect of hydroxyurea which increase zinc excretion as reported by Silliman et al., (1993).

Kaur M et al (2013) in their study on "the haemoglobinopathies and ratio of copper and zinc in sindhi community of Bhopal" found that zinc deficiency is common in haemoglobinopathic patients (thalassemia and sickle cell anaemia).

In the present study mean serum ferritin (ng/ml) level in thalassemia patients is more than sickle cell disease patients and are statistically highly significant ( $p < .0001$ ). The mean  $\pm$  S.D. of ferritin (ng/ml) in thalassemia patients is found to be  $1130.53 \pm 457.60$  ng/ml and that of sickle cell disease cases is  $620.92 \pm 359.76$  ng/ml.

In a study conducted by Nadeem Ikram et al., (2004) on "Ferritin Levels in Patients of Beta Thalassaemia Major" it was shown that mean serum ferritin levels was  $3390 \pm 135.6$  ng/ml.

Cunningham et al., (2004) reported mean serum ferritin levels in beta thalassemia patients of North America to be 1696 ng/ml (26).

However, Choudhry VP et al in India reported mean serum ferritin levels to be 6723 ng/ml (27)

In a study conducted by Mishra K Amit et al (2013) in Bhopal Madhya Pradesh on "Iron Overload in Beta Thalassaemia Major and Intermedia Patients" it was shown that the mean

serum ferritin level was  $2767.52 \pm 1849.1$  ng/ml which is quite higher than normal.

Another study by Mohammed Saied Abdulzahra et al (2009) "on Study of the effect of iron overload on the function of endocrine glands in male thalassemia patients" it was shown that the mean concentration of serum ferritin was more than eight times higher than normal.

Claster S et al<sup>15</sup> in their study found that mean ferritin level in thalassemia and sickle cell disease patients were  $3874 \pm 4451$  ng/ml and  $2089 \pm 1920$  ng/ml respectively and it was found to be statistically significant in both the groups ( $p < 0.02$ ).

## CONCLUSION

From the present study, it was observed that serum ferritin was significantly elevated in patients with haemoglobinopathies as compared to normal reference interval, however serum zinc was significantly decreased as compared to normal reference interval. Moreover, there was definite statistically negative correlation of serum ferritin to serum zinc. To conclude, measurement of zinc, ferritin in patients with haemoglobinopathies and replenishment of trace element in deficient states, by means of oral supplementation and removal of excess iron by chelation therapy could be a possible deterrent to the progression of disease. Regardless of the underlying etiology, these results suggest that all patients with thalassemia major and sickle cell disease who are repeatedly transfused should have periodic nutritional evaluation and supplementation as necessary.

However, as we are constrained by the limitation of time and relatively smaller sample size, it would probably be more predictive with larger sample size and longer period of study to explore more deep into this area for better management of the patients indisposed with haemoglobinopathies.

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## ORIGINAL RESEARCH PAPER

# A clinical study of hemothorax following blunt thoracic trauma

*Bhattacharyya DK<sup>1</sup>, Brahma RC<sup>2</sup>*

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### ABSTRACT

**Introduction:** Hemothorax following blunt thoracic trauma is a common occurrence. Prompt diagnosis and proper treatment is the key for good outcome. **Materials and methods:** This is a retrospective study carried out in Assam Medical College and Hospital over a period of two years from January 2017 to Dec 2018 to assess our management of hemothorax following blunt thoracic trauma. Hospital records of these patients were reviewed and analyzed. **Results:** Total 118 patients were admitted during this period in Assam Medical College & Hospital with diagnosis of hemothorax following blunt thoracic trauma. Male patients outnumbered female patients and road traffic accident was the main mechanism of blunt thoracic trauma. Chest pain was the main presenting symptom. 8(6.78%) patients with massive hemothorax were treated during primary survey. 12(10.17%) patients with small volume hemothorax were treated successfully by observation while observation failed in 3(2.54%) patients. 95(80.51%) patients with large hemothoraces were treated by Tube thoracostomy drainage after radiological confirmation. Eleven (9.32%) patients developed clotted hemothorax and required thoracotomy. Mortality rate of the present series was 2.54%. **Conclusion:** Hemothorax occurs frequently following blunt thoracic trauma. The Majority of these patients can be managed successfully by tube thoracostomy drainage only.

**Keywords:** Chest injury; traumatic hemothorax; thoracostomy; tube drainage; treatment.

### INTRODUCTION

Hemothorax is defined as collection of blood in pleural cavity. The most of the hemothoraces occur due to blunt or penetrating thoracic trauma. Iatrogenic manipulations also cause hemothorax. Spontaneous hemothorax results from medical causes.<sup>1</sup> Sources of blood in hemothorax may be from lung, chest wall, ruptures of pleural adhesions, mediastinum or peritoneal cavity through ruptured diaphragm.<sup>2</sup> Severity of hemothorax depends upon etiology

of bleeding into the pleural space, rate at which it occurs within pleural cavity and amount of blood that is collected there.<sup>3</sup> A study in a level I trauma center of United State found that blunt trauma is a major cause of thoracic trauma.<sup>4</sup>

Traditionally majority of hemothoraces are managed with tube thoracostomy drainage. However treatment advocated in the literature ranges from observation to various surgical interventions. When a hemothorax is not properly drained, retained hemothorax occurs. Its management also differs from authors to authors.<sup>5</sup>

The aim of the study is to review the management of patients admitted with diagnosis of hemothorax following blunt thoracic trauma and objective of the study is to analyze the outcome.

### MATERIALS AND METHODS

This was a hospital based retrospective study conducted in Assam Medical College & Hospital, Dibrugarh, Assam, India from January 2017 to December 2018.

Clinical details of the patients admitted during the above-mentioned period with hemothorax following blunt thoracic trauma were recorded from their case sheets and were analyzed with reference to their demographics, mode of injury, common presenting signs and symptoms, treatment offered to them, length of hospital stay, complications noted during the period and final outcome. Their follow-up records were reviewed for any residual symptoms and radiological findings.

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#### Address of Correspondence:

<sup>1</sup>Associate Professor

Unit of Cardiothoracic Surgery

**Mobile:** +919508263981 / +919435103148

**Email:** drdkbc@gmail.com

<sup>2</sup>Associate Professor (**Corresponding author**)

**Mobile:** +919864051733

**Email:** drrcbrahma@yahoo.com/ drdkbc@gmail.com

Department of Surgery

Assam Medical College, Dibrugarh, Assam, India

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**Inclusion criteria:** All hemothoraces following blunt trauma and above the age of 12 years.

**Exclusion criteria:** Patients who did not complete their treatment in hospital, penetrating injuries of the thorax and patient not giving consent for the study were excluded from the study. Hemothorax associated with laryngeal injuries, cervical injuries, esophageal or tracheal injuries were not included in the study.

RESULTS

A total of 118 patients with hemothorax following blunt thoracic trauma were admitted in Assam Medical College & Hospital, Dibrugarh over the period of two years from January 2017 to December 2018. 16 of them presented with bilateral while 102 of them had unilateral hemothorax.

Age of the patients in this study group ranged from 16 years to 74 years and average age noted was 42 years. In our study, 100(84.75%) patients were male and 18(15.25%) patients were female

72(61.02%) patients developed hemothorax following Road Traffic Accidents. Other mechanisms of injury recorded in the study were fall in 36(30.51%), physical assault in 8 (6.78%), occupational injury in 2(1.69%) patients (**Table 1**).

Table 1 Showing mechanisms of injury

Mechanism of injury	No. of patients	percentage
Road traffic accident	72	61.02%
Fall	36	30.51%
Physical assault	8	6.78%
Occupational injury	2	1.69%
Total	118	100%

48 patients (40.68%) of our hemothorax had associated pneumothorax.

The common presenting symptoms in our study were chest pain in 78(66.1%) and dyspnea in 62(52.5%) patients. Common physical signs noted were tenderness over the chest wall in 100 patients (84.74%), bone crepitation in 61(51.69%) patients and surgical emphysema in 39(33.1%).

In 13(11.02%) patients, hemothorax occurred without any rib fracture. One rib fracture was noted in 6 (5.08%) , 2 ribs fractures were noted in 16(13.56%) , and more than 2 rib fractures noted in 83(70.34%) patients. Of the 83 patients with more than 2 fractures,10(8.47%) patients presented with flail chest, 48(40.7%) had associated pneumothorax, 29 (24.58%) had pulmonary contusion and 20(16.95%) patients had other organs injury.

All admitted patients were administered with adequate analgesic, mucolytics, bronchodilators, and were encouraged for vigorous respiratory physiotherapy. Radiological

investigations were X-Ray of chest and CT scan of thorax. 8(6.78%) patients presented with massive hemothorax and were treated immediately in the casualty by placement of thoracostomy tube drainage. Radiological evaluations were done in them only after stabilizing their hemodynamic status. 1(0.85%) of these patients required emergency thoracotomy due to persistent bleeding.

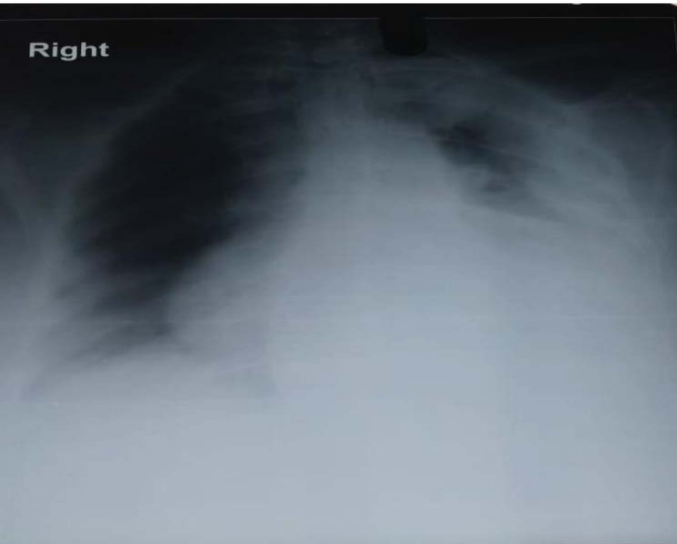


Figure 1 X-RAY Chest showing left hemothorax



Figure 2 CT Thorax showing left hemothorax

15(12.71%) patients with small volume hemothorax presented without any respiratory distress and were initially treated expectantly. Subsequently, 3(2.54%) of them developed respiratory distress and check X-ray established increment of hemothorax. They were treated with thoracostomy tube drainage. The average duration of hospital stay for those 12(10.17%) patients treated expectantly was 4.2 days and their hemothorax resolved completely in follow up visits.

In 95(80.51%) symptomatic patients, blood was evacuated from pleural cavity by large-bore tube thoracostomy. Of these 89 patients required unilateral and 6 patients required bilateral thoracostomy tube drainage. Average duration of thoracostomy drainage for them was 13.6 days and average duration of hospital stay was 16.1 days. In total 106(89.83%)

of our patients required tube thoracostomy drainage.

All hemothoraces were administered with first generation cephalosporin as prophylactic antibiotic and continued till removal of drainage tubes.

11(9.32%) patients developed retained hemothorax during the period and all of them required thoracotomy. Mortality of the present study was 2.54% (3 patients). All of them had multiple ribs fractures with significant hemothorax, massive pulmonary contusions and associated other organs injuries. 2 of them had flail chest and required ventilator support.

The discharged patients were followed up in OPD and follow-up period ranges from 1 month to 12 months. All complaints usually disappear within one month after discharge and follow-up chest X-ray did not show any residual collection.

## DISCUSSION

The exact incidence of hemothorax following trauma is unknown.<sup>6</sup> Average age of our patients was 41 years. Other studies also reported similar finding.<sup>7,8</sup> High incidence of hemothorax was found in male. Cause of male prominence in trauma is due to more involvement of male in outdoor activities like driving, industrial works, manual works than female.<sup>9,10</sup>

Similar to our findings, other studies have also found that the motor vehicle accident is the major mechanism of blunt thoracic trauma. Use of rapid means of transport and lack of knowledge about traffic rules are the main reasons behind it. Other mechanisms of injury noted were accidental fall or fall from height, assault, and industrial accidents.<sup>7,9</sup> Concomitant pneumothorax along with traumatic hemothorax is a frequent finding in thoracic blunt trauma. Incidence varies from study to study.<sup>4,11</sup>

Chest pain and dyspnoea are the most common symptoms at presentation<sup>8</sup> and tenderness over the chest wall, subcutaneous emphysema and bone crepitation were the most common findings on physical examination.<sup>8,9</sup>

In our study, we have noticed that with the increase in the number of rib fractures in hemothorax, associated complications like contusion of lung, flail chest, pneumothorax and other organ injury also increases. Similar finding was also noted by other authors.<sup>7</sup>

A massive hemothorax (>1.5 L of blood) is an immediate life threatening condition and has to be resuscitated during primary survey.<sup>12</sup> Indications accepted for emergency thoracotomy are (i) drainage of more than 1,500 mL of blood immediately after placement of tube thoracostomy. (ii) Continuous drainage of 150 mL/h to 200 mL/h for 2 hours to 4 hours after placement of thoracostomy tube. (iii) Requirement of persistent blood transfusion to maintain hemodynamic stability.<sup>13</sup> According to our record, eight (6.78%) patients with massive hemothoraces were treated during this period and one of them required emergency thoracotomy due to persistent bleeding.

X-ray of chest and Computed tomographic scan of thorax were performed to confirm the presence of hemothorax. Plain

X-ray of chest in standing posture requires a collection of more than 400 ml of blood to obliterate costophrenic angle while chest X-ray in supine position may not detect up to 1 liter of blood. CT scan of thorax is a better tool to detect hemothorax.<sup>13</sup>

Though many authors advocate tube thoracostomy drainage as initial treatment for all hemothoraces,<sup>13</sup> several retrospective studies support expectant management for the same.<sup>8,14,15</sup> Our expectant management was successful in 12 patients. Advantages of expectant management claimed are shorter length of hospital stay and reduced rate of empyema.<sup>14</sup>

106(89.83%) of our total patients with hemothorax were treated initially by tube thoracostomy drainage. It has been noted that about 60 to 90% of patients with chest injury can be managed by placement of thoracostomy tube.<sup>16</sup>

Some authors advocate Video-assisted thoracoscopic surgery (VATS) as initial treatment of hemothorax instead of tube thoracostomy. Advantages claimed are proper vision of pleural cavity, control of bleeding under direct vision, removal of any clot present inside thoracic cavity, possibility of correct placement of chest tube and post procedure short hospital stay.<sup>17-19</sup>

Use of antibiotics and duration of its use in hemothorax is controversial. Many authors do not find sufficient evidence to support its use while others recommend it.<sup>19,20</sup> We have used 1<sup>st</sup> generation cephalosporin from day of thoracostomy drainage till its removal.

Thoracentesis as a definitive treatment of a hemothorax is an obsolete intervention. The procedure is found to be associated with increased incidence of complications and high rate of failure.<sup>2,11</sup>

Eleven (9.32%) patients developed retained hemothorax. Reported incidence of retained hemothorax is about 0.5-30%.<sup>15</sup> One of the major complications of retained hemothorax is development of empyema, which are reported upto 50% of patients.<sup>21</sup> Incidence of empyema thoracic increases in retained hemothorax with increased in the number of rib fractures, increased in injury severity score and with increased number of attempts to drain retained hemothorax.<sup>22</sup>

Malposition of, and poor drainage through thoracostomy tubes results in retained hemothorax.<sup>23</sup> Treatments practiced for retained hemothorax are placement of a second thoracostomy tube, intrapleural fibrinolytic therapy, Video-Assisted Thoracoscopic Surgery (VATS) and thoracotomy.<sup>24</sup> However, second tube thoracostomy is associated with high failure rate and further surgical interventions are usually required for them at a later stage.<sup>25</sup> Fibrinolytic therapy is a non-operative method of evacuation of retained hemothorax and agents used for fibrinolytic therapy are streptokinase, urokinase and tissue plasminogen activator (TPA). Separate studies using streptokinase (250,000 units/ day) and urokinase (100,000 units/day) as fibrinolytic agents have achieved overall success rate of 92%.<sup>26,27</sup>

Our institution does not have any facilities for VATS. It is a safe procedure, is better tolerated than thoracotomy, and has



got less postoperative complications.<sup>22</sup> However, conversion to open thoracotomy may be required up to 17% cases.<sup>28</sup> VATS procedure requires single lung anaesthesia, which is not recommended in presence of hemodynamic instability. An obliterated pleural cavity due to previous infection or surgery is also a contraindication for VATS.<sup>29</sup>

We performed thoracotomy for all patients with retained hemothorax. Though thoracotomy is a more invasive procedure, it offers the best view of the intrathoracic collection than any other procedures to evacuate the clotted blood. Thoracotomy has been proved to be a procedure with the highest success rate as deinitive procedure for retained hemothorax and lowest need for additional therapy after the procedure.<sup>30</sup>

Our mortality rate was 2.54% (3 patients of hemothorax). A study in United State also recorded overall mortality rate of 4% in trauma victims.<sup>4</sup> All of them had severe chest injury along with other organ injuries. Studies have found that the severity of trauma is a determinant of mortality.<sup>9</sup>

## CONCLUSION

In conclusion, we can state that blunt thoracic trauma is a common cause of hemothorax. Road traffic accident is the most common mechanism, and most commonly affected gender is male. Small hemothoraces can be treated by observation. Initial treatment of a large hemothorax is thoracostomy tube drainage. Only massive hemothorax require immediate intervention during primary survey. Interventions for rest of the hemothoraces can be planned after radiological confirmation. The majority of hemothoraces do not require any major surgical procedures.

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**Contribution of Authors:** We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the contents of this article will be borne by the authors.

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## ORIGINAL RESEARCH PAPER

# A study of serum uric acid level in hypertensive patients

Baruah Rumi<sup>1</sup>, Baruah Bhaskar<sup>2</sup>, Baruah SK<sup>3</sup>, Saikia Nirmita<sup>4</sup>

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### ABSTRACT

**Background:** Various risk factors for development of hypertension, both modifiable and non modifiable, have been identified to aid in its prevention and management. In recent years, various studies have shown serum uric acid (UA) levels to be an independent predictor for developing hypertension. This study determined the uric acid level in hypertensive patients and established a relation between hypertension and uric acid level. **Materials and methods:** It was a case control study done from 1<sup>st</sup> March 2018 to 31<sup>st</sup> August 2018, which included a total of 80 newly diagnosed hypertensive cases and 80 normotensive controls matched for age and sex admitted in the Department of Medicine GMCH. The cases were classified into the various stages of hypertension as per the JNC-7 classification criteria. One way ANOVA analysis was performed to compare the differences in mean serum uric acid levels in the various categories. **Results:** The mean serum uric acid level among the controls was  $5.09 \pm 1.33$  mg/dl while among the cases was  $5.72 \pm 1.35$  mg/dl. Among the cases, mean serum uric acid in stage 1 and stage 2 HTN were  $5.15 \pm 0.97$  and  $6.35 \pm 1.45$  mg/dl respectively. There was statistically significant differences among the 3 groups, i.e. between stage 1 and stage 2 HTN, between control group and stage 1 HTN and between control group and stage 2 HTN, with a p value  $< .05$ . **Conclusion:** There was statistically significant differences between mean serum uric acid levels of newly diagnosed hypertensive cases and age and sex matched normotensive healthy controls and it tends to rise with the severity of hypertension.

**Keywords:** JNC 7; hyperuricemia; purine.

### INTRODUCTION

In the last two decades, the world has witnessed a significant increase in the prevalence of hypertension, one of the major and leading causes of cardiovascular disease. Studies have shown that each difference of 20 mm Hg of systolic and 10 mm of diastolic Hg was associated with twice the risk of

death from heart disease, stroke or other cardiovascular disease.<sup>1</sup>

Various risk factors for development of hypertension, both modifiable and non modifiable, have been identified to aid in its prevention and management. In recent years, various studies have shown serum uric acid (UA) levels to be an independent predictor for developing hypertension. In India, not many studies are available regarding the association of hypertension and hyperuricemia. This study has been done to assess the level of serum uric acid in hypertensives and to ascertain whether there is a relation between hyperuricemia and hypertension.

Uric acid is a byproduct of purine metabolism produced in blood from endogenous purine (2/3) substances or from diet (1/3). The amount of urate in the body is affected by the balance of its production and excretion. Alcohol and high-purine foods consumption, low water consumption and poorly exercising are contributing factors responsible for hyperuricemia. Hyperuricemia is defined as a level of serum uric acid level over 7.0 mg/dL.<sup>2</sup>

Uric acid is commonly associated with hypertension. It is present in 25% of untreated hypertensive subjects, in 50% of subjects taking diuretics, and in 75% of subjects with malignant hypertension.<sup>3</sup> The association of hyperuricemia

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#### Address for correspondence:

<sup>1</sup>Associate professor

**Mobile:** +919435015669

**Email:** baruah-rumi@yahoo.co.in

Department of Anesthesiology

Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta

<sup>2</sup>Associate professor (**Corresponding Author**)

**Mobile:** +919864012000

**Email:** bhaskarbaruah1@yahoo.com

<sup>3</sup>Professor and Head, <sup>4</sup>Post Graduate Trainee

Department of Medicine

Gauhati Medical College and Hospital, Guwahati

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with hypertension has long been recognized with early investigators such as Frederick Mahomed, Alexander Haig, and Nathan Smith Davis, hypothesizing that uric acid might be a cause of hypertension or renal disease.<sup>4</sup> Uric acid is thought to play a pathogenic role in hypertension mediated by several mechanisms such as inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of the renin – angiotensin – aldosterone system.<sup>5</sup>

This paper has aimed to study the level of serum uric acid in hypertensive patients and to know the relation in-between.

## MATERIALS AND METHODS

The study was a case control study done from 1<sup>st</sup> March 2018 to 31<sup>st</sup> August 2018. It included a total of 80 newly diagnosed hypertensive cases and 80 normotensive controls matched for age and sex admitted in the Department of Medicine GMCH. The cases were classified into the various stages of hypertension as per the JNC-7 classification criteria. Blood pressure has been recorded as the average of 2 or more readings at each of the 2 or more visits after initial screening.<sup>6</sup> All the patients were subjected to relevant clinical examinations and laboratory investigations to look for secondary causes of hypertension. All other causes of secondary hypertension were ruled out. Reference Values for Serum Uric Acid levels – 7 mg/dl.<sup>3</sup>

**JNC -7 classification of hypertension<sup>7</sup>** used in this study.

BLOOD PRESSURE	SYSTOLIC BP	DIASTOLIC
STAGING	(mm Hg)	BP(mm Hg)
NORMAL	<120	AND <80
PREHYPERTENSION STAGE 1	120-139	OR 80-89
HYPERTENSION STAGE 2	140-159	OR 90-99
HYPERTENSION	>160	OR >100
ISOLATED SYSTOLIC HYPERTENSION	>140	AND <89

## Statistical analysis

Data was recorded into a preformed and pretested proforma. Statistical analysis was done by MS excel 07 and GRAPHPAD INSTAT software. Data are expressed as mean and standard deviation. One way ANOVA analysis with post test was performed to compare the differences in mean serum uric acid levels in the various categories.

Inclusion criteria: (i) Age >18 years; (ii) Newly detected patients of essential hypertension.

Exclusion criteria: (i) Patients with gout; (ii) Patients on uricosuric drug; (iii) Patients on drugs which increase serum uric acid level e.g salicylates (>2gm/day), diuretics,

ethambutol, Pyrazinamide, etc other than uricosuric drug; (iv) Patients with renal failure; (v) Lymphoproliferative or myeloproliferative disorders; (vi) Secondary hypertension and pregnancy induced hypertension.

## RESULTS

In the present study, out of 80 controls, 57.5% were males and 42.5% were females while among the 80 cases, 45(56.25%) were males and 35(43.75%) were females (**Table 1**).

**Table 1** Sex distribution in study group

		TOTAL	PERCENTAGE(%)
CONTROL	MALE	46	57.5
	FEMALE	34	42.5
CASE	MALE	45	56.25
	FEMALE	35	43.75

In the present study, out of 80 cases, 42 patients had stage 1 hypertension and 38 had stage 2 hypertension. Out of 42 cases of stage 1 HTN, 24 were males and 18 were females, while among the 38 cases of stage 2 HTN, 21 were males and 17 were females (**Table 2**).

**Table 2** Sex distribution according to stage of hypertension

	MALE	FEMALE	TOTAL
STAGE 1	24	18	42
STAGE 2	21	17	38

The mean serum uric acid level among the controls was 5.09±1.33 mg/dl while among the cases was 5.72±1.35 mg/dl. There was statistically significant difference between the two groups (p value<.05) (**Table 3**).

**Table 3** Mean serum uric acid level in controls and cases

	CONTROL	CASES
MEAN±SD(mg/dl)	5.09±1.33	5.72±1.35

In the present study, mean serum uric acid level in controls was 5.09±1.33mg/dl while among the cases was 5.72±1.35 mg/dl. Mean serum uric acid in stage 1 and stage 2 HTN were 5.15±0.97 and 6.35±1.45 respectively (**Table 4**). There was statistically significant differences among the 3 groups, i.e between stage 1 and stage 2 HTN, between control group and stage 1 HTN and between control group and stage 2 HTN, with a p value <.05.

**Table 4** Mean serum uric acid in controls and cases (according to stage of hypertension)

value	CONTROLS	STAGE 1 HTN	STAGE 2 HTN	P
MEAN (mg/dl)	5.09±1.33	5.15±0.97	6.35±1.45	<0.05



## DISCUSSION

The mean serum uric acid level among the controls was  $5.09 \pm 1.33$  mg/dl while among the cases was  $5.72 \pm 1.35$  mg/dl. Among the cases, mean serum uric acid in stage 1 and stage 2 HTN were  $5.15 \pm 0.97$  and  $6.35 \pm 1.45$  mg/dl respectively.

This result is similar to those of Neki et al<sup>8</sup> and Perlstein et al<sup>9</sup> who reported a mean uric acid level of  $5.8 \pm 1.3$  mg/dl and  $5.8 \pm 0.9$  mg/dl respectively in the hypertensive patients. Similar results were documented by Strasak et al<sup>10</sup> and Kashem et al<sup>11</sup> ( $5.7 \pm 1.2$  and  $5.8 \pm 1.5$  mg/dl respectively). Raina S et al also found the mean serum uric acid level was significantly higher in the cases ( $5.5 \pm 1.7$  mg/dl) than in the controls ( $4.9 \pm 1.1$  mg/dl;  $P < .05$ ), which is similar to our result.<sup>12</sup>

In a similar study by Reddy et al, it was reported the mean serum uric acid levels were found to be  $4.78(2.32)$  mg/dl,  $4.42(1.38)$  mg/dl,  $6.57(1.55)$  mg/dl and  $4.44(1.44)$  mg/dl in controlled hypertension, stage 1 hypertension, stage 2 hypertension and isolated systolic hypertension respectively. There was significant difference between stage 2 hypertension with the stage 1 hypertensive, isolated systolic hypertensive and well controlled hypertensive patients with the p values of .001, .001 and .002 respectively.<sup>4</sup>

N. S. Neki and Tamilmani, in a case control study comprising of a total of 200 essential hypertensive patients, categorized into Stage 1 or Stage 2 hypertension (based on JNC VII classification) and 200 normotensive controls also observed that the value of mean SUA (serum uric acid) was 5.8 mg% in cases and 4.4 mg% in the control group. The mean values of SUA were 5.37 mg% & 6.39 mg% respectively in stage-1 & stage-2 HTN, which was statistically significant and in consistent with the results of the present study.<sup>8</sup>

Ouppatham S et al in their study of 5,564 subjects, observed a significant and positive correlation both between serum uric acid and SBP( $r=0.186$ ,  $P < .001$ ) and between serum uric acid and DBP( $r=0.255$ ,  $P < .001$ ).<sup>13</sup>

Poudel B et al<sup>14</sup> and Shrivastav et al<sup>15</sup> also found higher levels of serum uric acid levels in newly diagnosed hypertensive patients as compared to healthy normotensive individuals.

Lee et al<sup>16</sup> also found a positive correlation between hyperuricemia and hypertension.

Ankit Vakil et al studied 100 patients and found that in stage 1 HTN out of 28 patients, 21 patients have high SUA level, while in stage 2 HTN out of 72 patients, 44 patients have high SUA level. They found that there is definite relation in SUA levels between hypertensive patients and normotensive patients and there is a directly proportional relation in the levels of SUA in relation to the duration and severity of hypertension.<sup>17</sup>

In a similar study by Mishra et al, statistically significant difference (p value  $< .05$ ), was found between mean serum uric acid of newly diagnosed hypertensive cases and normotensive healthy controls.<sup>18</sup>

Mangesh Tiwaskar in his study of 100 patients found a

positive correlation between hyperuricemia and hypertension in newly diagnosed hypertensive patients.<sup>19</sup>

## CONCLUSION

Although, serum uric acid levels were found to be within the normal range, there was statistically significant differences between mean serum uric acid levels of newly diagnosed hypertensive cases and age and sex matched normotensive healthy controls and it tends to rise with the severity of hypertension. However, further studies with a larger sample size is required to arrive at a definite conclusion.

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**Ethical Clearance:** Taken.

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## ORIGINAL RESEARCH PAPER

# Relationship between body mass index with eruption of third permanent molar teeth

*Deka SJ<sup>1</sup>, Mahanta Putul<sup>2</sup>, DOUNGEL Nomi<sup>3</sup>, Bora Neelutpal<sup>4</sup>, Dutta Jahnobi<sup>5</sup>, Thakuria KD<sup>6</sup>*

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## ABSTRACT

**Objective:** The aim of the study is to investigate the relationship between the nutritional status and the permanent eruption of the third molar teeth aged 13-26 years.

**Introduction:** It is known that chronology of dental development is less variable than the bone development and the method applied for this particular period of life is a reliable indicator of age. Though eruption of teeth may be affected by dietary variation, the eruption time for teeth are fairly constant. **Materials and methods:** It is a cross-sectional prospective study conducted among the people aged 13-26 years through a questionnaire over 100 participants. **Results:** A total of 51% male and 49% female were participated in this study. Out of 25 participants of complete third molar eruption, majority 52% (13) participants were belonging to female. In this study, the percentage of complete third molar eruption among the participants with different Body Mass Index (BMI) categories like underweight, normal and overweight were 7, 16 and 2 respectively. **Conclusion:** These findings suggest a relationship between nutritional status with eruption of third permanent molars. As the complete eruption of third molar is less with underweight and obese individuals, initiatives should be undertaken for health promotion among the common people regarding oral health and healthy eating.

**Keywords:** Height; weight; dentition; obesity; malnutrition.

## INTRODUCTION

One of the greatest problems for India is undernutrition among children. Malnutrition, the condition resulting from faulty nutrition, weakens the immune system and causes significant growth and cognitive delay. Growth assessment is the measurement that best defines the health and nutritional status of children.<sup>1</sup> A balanced diet contains all the elements is very necessary for the growth of the teeth.<sup>2</sup> So, nutritional

deficiencies can delay the process of eruption of permanent teeth.<sup>3</sup>

On the other hand, dental development is relatively independent from another systems of maturation.<sup>4</sup> Though eruption of teeth may be affected by dietary, climatic, racial and geographical variation, the eruption time for deciduous and permanent teeth are fairly constant. Eruption of teeth is one of the changes observed easily among the various dynamic changes that occur from formation of teeth to the final shedding of it. There is a significant time lag between cutting of a tooth into the mouth and completion of eruption of teeth.<sup>5</sup>

As it is a debatable to know whether nutritional status has any role in the process of dentition or not, this paper has aimed to know the relationship between the nutritional status with eruption of permanent third molar teeth of aged 13-26 years.

## MATERIALS AND METHODS

It is was a cross-sectional prospective study conducted over 100 participants aged 13-26 years. Here, we have investigated

### Address for correspondence

<sup>1</sup>Associate Professor

**Email:** subha.deka@gmail.com

**Mobile:** +919435338109

<sup>2</sup>Professor

Department of Forensic Medicine and Toxicology  
Assam Medical College and Hospital, Dibrugarh, Assam, India

<sup>3</sup>Associate Professor (**Corresponding Author**)

Physiology, Tezpur Medical College, Tezpur, Assam, India

**Email:** nomidoungel@gmail.com

**Mobile:** +919864071754

<sup>4</sup>Registrar, <sup>5</sup>Lecturer, Department of Dentistry, Govt. Dental  
College, Dibrugarh, Assam and India

<sup>6</sup>Assistant Professor of Physiology, TMC, Tezpur, Assam

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eruption of permanent third molar teeth in relation to nutritional status along with some co-variants with the help of a pre-designed and pre-tested questionnaire, anthropometric measurements and clinical examination of the participants in the year 2019 in Assam Medical College, Dibrugarh, Assam and India.

Prior to collection of the data, Human Institutional Ethical Clearance was taken which included informed consent of

the participant. The data thus collected were analyzed using Microsoft Excel software.

## RESULTS

A total of 51% male and 49% female were participated in this study of evaluation of permanent third molar eruption (TME) and its relationship with the nutritional status. The age and sex wise distribution of cases are shown in **Table 1**.

**Table 1** Distribution of the study participants according to age and sex

Age (in Years)	Male		Female		Total	
	No.	%	No.	%	No.	%
13	1		3		4	4
14	6		13		19	19
15	14		9		23	23
16	5		2		7	7
17	2		1		3	3
18	1		1		2	2
19	2		2		4	4
20	2		2		4	4
21	5		5		10	10
22	3		2		5	5
23	4		3		7	7
24	2		3		5	5
25	3		1		4	4
26	1		2		3	3
Total	51	51.0	49	49.0	100	100

In this study, 50% cases showed no eruption where as 25% cases showed complete TME. Out of 25 cases of complete

TME, 52% (13) cases were belong to female. TME was more 18% (18) common in lower jaw. Details are shown in **Table 2**.

**Table 2** Status of TME in Male and Female in different quadrant of Jaw

Status of Eruption	Overall		Male		Female		p-value
	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	
No Eruption	50	14.62 $\pm$ 0.88	24	14.96 $\pm$ 0.91	26	14.31 $\pm$ 0.74	0.007
UL	1	----	0	----	1	----	----
UR	3	16.00 $\pm$ 1.73	3	16.00 $\pm$ 1.73	0	----	----
Both Upper	0	----	0	----	0	----	----
LL	1	----	1	----	0	----	----
LR	2	17.50 $\pm$ 3.54	1	----	1	----	----
Both Lower	18	20.72 $\pm$ 2.49	10	21.40 $\pm$ 2.27	8	19.88 $\pm$ 2.64	0.206
Complete Eruption	25	22.92 $\pm$ 1.94	12	22.83 $\pm$ 1.99	13	23.00 $\pm$ 1.96	0.835



UL – Upper left, UR- Upper right, LL- Lower left, LR- Lower right

The mean age of completion of TME in male is 22.92 years

and in female it is 23 years although earliest TME was at 20 years of age and that too in female and completed by 25 years in both the sexes as shown in **Table 3**.

**Table 3** Mean age at completion of TME in Male and Female

Status	Overall		Male		Female		p-value
	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	
Incomplete Eruption	75	16.32 $\pm$ 3.01	15	16.79 $\pm$ 3.14	10	15.81 $\pm$ 2.81	0.156
Complete Eruption	25	22.92 $\pm$ 1.94	12	22.83 $\pm$ 1.99	13	23.00 $\pm$ 1.96	0.835

**Table 4** Mean age at Eruption of permanent 3<sup>rd</sup> molar teeth in upper and lower jaw

	Upper Jaw		Lower Jaw		p-value
	No.	Mean $\pm$ SD	No.	Mean $\pm$ SD	
Either Left or Right	2	18.00 $\pm$ 00	2	19.50 $\pm$ 0.71	-----
Both Left & Right	18	20.72 $\pm$ 2.49	0	-----	-----

In **Table 4**, mean age at eruption of third molar in upper and lower jaw are shown as a comparison.

## DISCUSSION

Public health issues and nutritional imbalances of the people of Assam, living in this part of the Nation still needs special attention.

Out of 100 participants of this study, 25%(25) shows complete TME in all quadrants where female outnumbered by 52%(13), over male 48%(12). TME was more 18%(18) in both lower jaw. This finding is in strong agreement with a study carried out by Mahanta P. In his study, it was revealed that earliest TME to be in female at 16 year and completed by 24 years in both the sexes and that too in lower jaw in both the sexes.<sup>6,7</sup>

Many other studies on TME it was concluded that it erupts earliest by 16-17 years and that too in female and one year later in male and completed by 24 years in both the sexes. This findings of third molar eruption between 16-25 years are well tallied with the findings of Gorden et al<sup>8</sup>, Scot<sup>9</sup>, Polson<sup>10</sup>, Smith<sup>11</sup>, Kerr<sup>12</sup>, Grewal<sup>13</sup>, Savara and Steen<sup>14</sup>, Tedeschi et al<sup>15</sup>, Hassanali<sup>16</sup>, Hagg and Taranger<sup>17</sup>, Pathak et

al<sup>18</sup>, Rao<sup>19</sup>, Vij<sup>20</sup>, Korhonen et al.<sup>21</sup> and Chaurasia.<sup>22</sup> Although, the female preponderance of TME and its completion time are tallied with those findings, yet it differ in earliest TME time with the present study. These discrepancies with the current study may be because of a smaller number of study participants and different geographical areas, etc.

The mean age of TME in both left and right quadrant was 20.72 years. TME is more (**20%**) in average economic group (BG Prasad's Social Class II).

In this study the percentage of complete TME among the participants with different BMI categories like underweight, normal and overweight were 7, 16 and 2 respectively. This high percentage of complete TME with the participant of normal BMI (p-value=0.002) is an agreement with a study conducted by Alhamda Syukra.<sup>3</sup> However, incomplete TME was more (35%) with the underweight participants signifying the needs of good nutrition for appropriate dentition, etc. Malnutrition and poor nutrition in early childhood affects tooth eruption. This finding is also supported by Eskeli R et al.<sup>23</sup>

The relation of TME with Socio-demographic variables are shown in **Table 5** with **BMI**.

**Table 5** Relation of Eruption of permanent 3<sup>rd</sup> molar teeth with Socio-demographic variables

Variables		Incomplete Eruption	Complete Eruption	p-value
Age (in years)	13	4	0	0.000
	14	19	0	
	15	23	0	
	16	7	0	
	17	3	0	
	18	2	0	
	19	4	0	
	20	2	2	
	21	4	6	
	22	2	3	
	23	2	5	
	24	3	2	
	25	0	4	
	26	0	3	
Sex	Male	39	12	0.819
	Female	36	13	
Place of Residence	Rural	15	12	0.006
	Urban	60	13	
Economic Status	I	10	4	0.000
	II	10	20	
	III	23	1	
	IV	32	0	
History of Disease	Yes	0	0	-----
	No	75	25	
BMI	Underweight	35	7	0.002
	Normal	31	16	
	Overweight/Obese	9	2	
Height in cm	140-150	13	4	0.171
	150-160	32	5	
	160-170	23	12	
	170-180	7	4	
Weight in kg	40-60	66	16	0.015
	60-80	9	8	
	Above 80	0	1	

and Alvarez et al.,<sup>24</sup> though a study done by Boenjamin et al. in Jakarta showed no association between nutritional status with the eruption of permanent third molar teeth.<sup>25</sup>

## CONCLUSION

The present study showed a significant association between Body Mass Index with the eruption of third molars in Dibrugarh City. On comparing the eruption of third molar

teeth in both the sexes, female showed an overall earlier eruption than males. Further, participant who were underweight and over weight were found to have delay in eruption of third molar teeth than participant with normal BMI. Hence, in future, longitudinal and multicentric researches are recommended with wide range of participants to determine the trends in the eruption of third molar teeth among Assamese population.

**Limitation:** Number of participants should have been larger. A good number of participants is necessary to opine about TME in some variables with accuracy.

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## CASE REPORT

# Sudden death during liposuction surgery: a rare occurrence

DebBarma Antara<sup>1</sup>, Dey Arijit<sup>2</sup>, Yadav Abhishek<sup>3</sup>, Prasad Kulbhushan<sup>4</sup>, Gupta SK<sup>5</sup>

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## ABSTRACT

*Liposuction is a cosmetic surgery which is gaining popularity in present day modern world. This procedure is considered to be safe and very rarely leads to fatality. The authors report a rare case of Intra-operative death due to fat embolism during liposuction operation. The deceased had minimal pre-diagnosed risk factors for developing the complication while undergoing abdominal liposuction. Autopsy revealed hematoma over pericardium with luminal blockade of all coronary vessels. Hematoma and fat coagulum mixed masses were spread in between the peritoneal wall and subcutaneous tissue and. Histopathology examination of lungs and brain were done where fat embolism was present in lungs and meningeal vessels. Fat embolism syndrome (FES) is a life-threatening condition which has been described in patients after liposuction both mechanically and biochemically. Sudden deaths in a surgical procedure such as liposuction can easily lead to allegations of medical negligence. A thorough autopsy, along with histopathological examination can reveal the actual cause of death, as evident in this case. The authors aim to increase the awareness of public and Medical profession regarding the fatal complication of aesthetic procedures which are considered generally harmless.*

**Keywords:** Fat embolism syndrome; Pulmonary fat embolism; Cosmetic Surgery.

## INTRODUCTION

Liposuction is a surgical technique that improves the body's contour by removing excess fat deposits located between the skin and muscle and is a commonly performed aesthetic procedure.<sup>1</sup> Although it is considered as a procedure with few clinical side effects, the increasing popularity of liposuction brings more frequent reports of related complications. According to an American Society for Aesthetic Plastic Surgery survey,<sup>2</sup> the complication rate per 100,000 liposuctions performed by plastic surgery specialists

is 0.25%, while the mortality rate is 0.002%. Fat embolism is one of the most serious complications in liposuction. It can result from cosmetic surgery such as liposuction and/or fat grafting, cardiopulmonary bypass, pancreatitis, joint repair, severe burns, sickle cell anemia, diabetes mellitus, and lipid parenteral infusion.<sup>3,4</sup> The overall mortality from FES after liposuction is approximately 10–15%<sup>5</sup> with higher mortality associated with fulminant FES due to severe right heart failure compared with FES in which the mortality relates largely to underlying respiratory failure (or rarely cerebral edema causing brain death).<sup>6</sup> We report a case of a fatal outcome of a massive fat embolism in a young individual during the intra-operative period of an abdominal liposuction resulting in embolic stroke and sudden death. The authors aim to increase the awareness of public and medical profession regarding the fatal complication of aesthetic procedures which are considered generally harmless.

## Case history

A 34 year old male with body weight 94 kg and BMI 32.2 kg/m<sup>2</sup> with history of hypothyroidism was admitted to a hospital with diagnosis of resistant abdominal fat, to undergo liposuction from abdomen, back and face. Prior to the operation, a detailed informed consent was taken, where risk of fat embolism was mentioned. Pre operative Anesthetic check-up was done, which included routine blood tests, Echocardiography, chest X ray, ECG and all were within normal limits. During operation, under General Anesthesia,

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## Address for correspondence:

<sup>1</sup>Senior Medical Officer (**Corresponding author**)

**Email:** antaradebbarma@gmail.com

**Mobile:** +919205623401

<sup>2</sup>Senior Resident, <sup>3</sup>Assistant Professor, <sup>4</sup>Professor & Head Department of Forensic Medicine and Toxicology, All India Institute of Medical Sciences (AIIMS), New Delhi-110029

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3.5 liters of tumescent was injected and abdominal liposuction done on the abdomen, back and flanks and around 4.5 liters of fat was removed. At the end of liposuction operation, patient started de-saturating, became unconscious suddenly and suffered a cardiac arrest immediately. Patient was transferred to a nearby super specialty hospital, where he was declared to be brought dead.

### Autopsy findings

Autopsy was performed in Department of Forensic Medicine, All India Institute of Medical Sciences (AIIMS), New Delhi. There were surgical bandages present over lower part of face, right flank, both gluteal regions, lower part of anterior chest and abdominal walls. Multiple surgically created punctured wounds were present below both nipples, just above umbilicus, bilaterally over inguinal area and over both flanks (**Figure 1**).



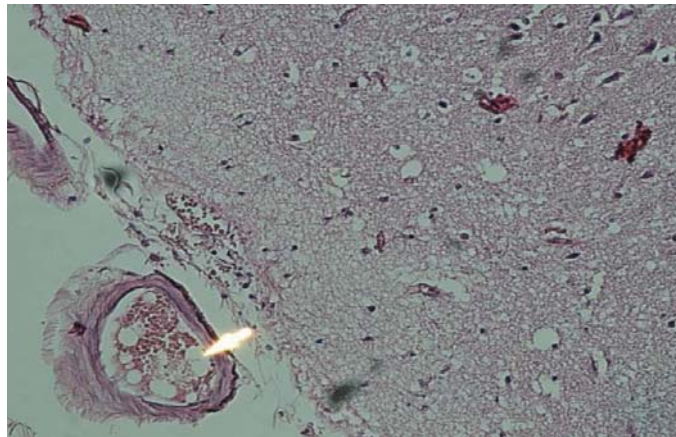
**Figure 1** Multiple surgically created punctured wounds were present below both nipples, just above umbilicus, bilaterally over inguinal area and over both flanks.



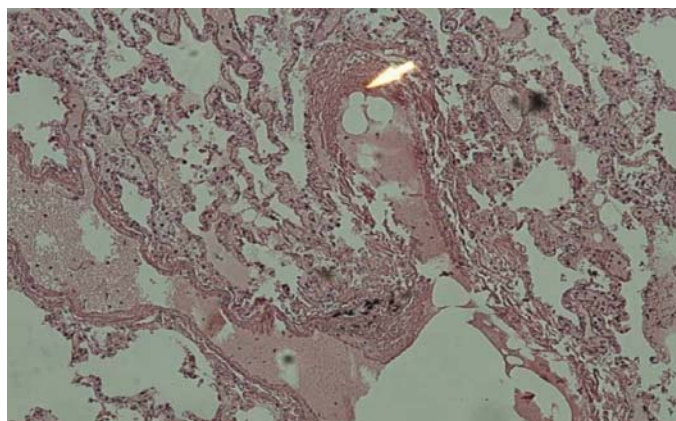
**Figure 2** Subcutaneous fat of thoracic and peritoneal cavity was turned into hemorrhagic and fibrotic mass

Subcutaneous fat of thoracic and peritoneal cavity was turned into hemorrhagic and fibrotic mass (**Figure-2**). Liver was enlarged, with hepatic steatosis. Heart showed 90% stenosis of left anterior descending and right circumflex artery along

with a haematoma over pericardium. Histopathology revealed mild edema of brain parenchyma and fat embolus in meningeal vessels. Pulmonary alveolar spaces were partially collapsed and fat embolus was present in pulmonary blood vessels (**Figure 3 and 4**). The cause of death was opined as cerebral and pulmonary embolism during liposuction operation.



**Figure 3** Histopathology confirms fat embolus present in cerebral blood vessels.



**Figure 4** Histopathology confirms fat embolus present in pulmonary blood vessels.

### DISCUSSION

Liposuction is a very common cosmetic surgical procedure nowadays that consists of removal of excess fatty tissue from healthy bodies, done under general or local anesthesia according to the extent of the area to be treated.<sup>7</sup> Intervention may be performed using various surgical techniques: Wetting solution techniques, standard liposuction or suction-assisted lipoplasty, internal ultrasound-assisted liposuction, VASSER-assisted liposuction, external ultrasound-assisted liposuction, LASER-assisted liposuction, power-assisted liposuction and Vibro liposuction.<sup>8</sup> Minor complications following liposuction include seroma, hematoma, hyper-pigmentation and penile or vulvar swelling. The serious major complications include sepsis,<sup>9</sup> perforation of abdominal or thoracic viscera,<sup>10,11</sup> hemorrhage, hypotension,<sup>12</sup> pulmonary embolism,<sup>13</sup> fat embolism,<sup>14</sup> pulmonary edema and cardiac arrest<sup>15</sup>. In the case reported here, the plastic surgery hospital used the

wetting solution technique in liposuction, which destroys the cytomembrane of the subcutaneous fat cell using the injection of isotonic or hypotonic normal saline into the operative site prior to liposuction. The level of surgical influence on the body is directly relative to the fat suction volume, surgical scope, and patient's general condition. Large volume and multi-position liposuction causes pulmonary and cerebral embolism, postoperative infection, and left lower limb deep venous thrombosis. If the fat tissue is badly damaged and surpasses the ability of plasma to decompose, substantial amounts of free fat enter the blood and cause Fat Embolism Syndrome (FES), which is the most significant complication causing mortality in liposuction.<sup>16</sup>

There is no specific therapy for FES, so prevention, early diagnosis, and supportive therapies are very important. Prevention of FES should include careful selection of patients and techniques, reduction of surgical time and the amount of fat aspirated and postoperative close observation and patient monitoring with intravenous fluid treatment for a minimum of 24 hour postoperatively.<sup>17,18</sup> FES is a self-limiting disease with respiratory distress, so therapeutic measures are aimed at improving respiratory conditions during the disease. Low-molecular-weight dextran is helpful to decrease blood viscosity, reduce platelet adhesion, reverse thrombocytopenia and reduce cell aggregation. Also, steroids are used extensively, as they limit the increase of FFAs, diminish the inflammatory response, inhibit complement-mediated leukocyte aggregation, protect capillary integrity and minimize interstitial edema accumulation.

## CONCLUSION

FES occurring in surgical liposuction can be rapidly fatal as evident from this case. The Surgeons and Anesthesiologists should be aware and prepared for early diagnosis and treatment. Minimum conditions of operation theatre infrastructure and ICU backup required should be ensured for unforeseen complications. Surgical aesthetic procedures should preferably be performed in Tertiary care hospitals with optimum diagnostic and therapeutic resources in cases of such operative complications.

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## CASE REPORT

# Emerging infections: shewanella in lactational breast abscess

Sharma Mitrajit<sup>1</sup>, Das PK<sup>2</sup>, Das PP<sup>3</sup>, Malakar Jaydeep<sup>4</sup>

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### ABSTRACT

*Shewanella* spp. is saprophyte bacteria that are part of the marine microflora in warm climates and they are rarely pathogenic. In recent times, the incidence of *Shewanella* infections is in the rising trend. In humans, it is mostly isolated from cellulitis, abscesses, bacteremia and wound infections and with no literature suggesting its isolation from lactational breast abscess. The case was managed by incision and drainage with proper antibiotic coverage. This case study suggests that *Shewanella* infection is more widespread and not just limited to coastal areas, with exposure to sea water and marine product ingestion. In addition, the unexpectedly multi-drug resistant isolate raises concern.

**Keywords:** Rare pathogen; emerging bacteria; Vibrionaceae; *Shewanella putreficans*; imipenem resistant; breast infection.

### INTRODUCTION

Lactational breast abscess is defined as a localized collection of pus within the breast during the period of lactation. It is most often a complication of lactational mastitis which is an inflammation of breast tissue secondary to stasis of milk and bacterial colonization, mostly staphylococcus.<sup>1</sup> *Shewanella* spp. is unusual cause of abscess in humans with no report of its isolation from breast abscess. It is a saprophytic, gram negative rod, belonging to the family Vibrionaceae. It is oxidase and catalase positive, non fermenter that produces hydrogen sulphide.<sup>2</sup> This ubiquitous organism has been isolated from many foods, sewage and both fresh and salt water. There are several reports describing this organism causing human infections, such as cellulitis, abscesses, bacteremia and wound infections.<sup>3</sup>

Here, we report a rare case of isolation of *Shewanella putrefaciens* from a sample of lactational breast abscess in a patient without recent contact with aquatic environment and/or consumption of products of marine origin, suggesting a more widespread distribution of pathogenic *Shewanella* spp.

in warm tropical areas.

### CASE STUDY

A 20 year lactating mother reported to the emergency with left sided engorgement of breast, with redness and swelling,



**Figure 1** Abscess after incision and drainage and debridement

### Address for correspondence:

<sup>1</sup> PGT

**Mobile:** +919706582392

**Email:** mitrajitsurgery@gmail.com

<sup>2</sup> Assistant Professor

<sup>3</sup> HOD and Professor **Corresponding author**

**Mobile:** 9365286091

**Email:** ppdasdr@gmail.com

<sup>4</sup> PGT, Department of General Surgery  
Gauhati Medical College and Hospital

**Email:** jmala4@gmail.com

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with associated fever and chills. Ultrasound showed multiloculated collections in right upper inner quadrant with abscess measuring 6 X 7 cms in dimension. It was managed with incision and drainage and pus was sent for culture (**Figure 1**). The culture report came positive for (91%) *Shewanella putrefaciens* (done in VITEK 2 automated

identification and antibiotic testing system). It was imipenem resistant with sensitivity shown to Aztreonam, Minocycline, Tigecycline, Colistin (**Figure 2**). She was started on Colistin, supported by breast emptying and regular dressing with a placental extract gel. She recovered well, defect was closed using Ethilon 2-0 c and the patient is on followup.

Organism Quantity:  
Selected Organism : *Shewanella putrefaciens*

Source: BREAST ABSCESS/S

Collected: Jan 4, 2019

Comments:	As per joint statement from CLSI-EUCAST 2017, BMD or Broth microdilution is the only approved method for testing Colistin sensitivity
	Method: Test done in Vitek2 compact automated identification and antibiotic sensitivity testing system.
	KINDLY CORRELATE THE REPORT CLINICALLY.

Identification Information	Analysis Time: 6.80 hours	Status: Final
Selected Organism	91% Probability Bionumber: 5072201110740020	<i>Shewanella putrefaciens</i>
ID Analysis Messages		

Susceptibility Information			Analysis Time: 9.97 hours			Status: Final		
Antimicrobial	MIC	Interpretation	Antimicrobial	MIC	Interpretation	Antimicrobial	MIC	Interpretation
Ticarcillin/Clavulanic Acid	>= 128	R	Amikacin	>= 64	R			
Piperacillin/Tazobactam	>= 128	R	Gentamicin	>= 16	R			
Ceftazidime	>= 64	R	Ciprofloxacin	>= 4	R			
Cefoperazone/Sulbactam	>= 64	R	Levofloxacin	2	S			
Cefepime	32	R	Minocycline	<= 1	S			
Aztreonam	<= 1	S	Tigecycline	<= 0.5	S			
Imipenem	>= 16	R	Colistin	<= 0.5	S			
Meropenem	>= 16	R	Trimethoprim/Sulfamethoxazole	>= 320	R			

+= Deduced drug \* = AES modified \*\* = User modified

**Figure 2** The culture sensitivity report of the case

## DISCUSSION

*Shewanella* spp. have been associated with several kinds of infections like biliary tract infections, empyema, skin and STIs such as fulminant periorbital facial cellulitis, dacrocystitis, perianal abscess, finger abscess, traumatic lesions or burns of lower limbs, bacteremia and rheumatic heart diseases. It has also been reported in premature babies with pneumonia.<sup>4</sup> This, according to us, is the first case of *Shewanella* isolation from lactational breast abscess. It is mostly reported from ear infections, followed by cellulitis, diabetic foot ulcers, necrotizing fasciitis, myonecrosis. This case adds to an emerging infection from Indian Subcontinent which has relatively less reported cases in comparison to the European Countries. The isolate came sensitive to Aztreonam ( $\leq 1$ ), Minocycline ( $< 1$ ), Tigecycline ( $\leq 0.5$ ) and Colistin ( $d''0.5$ ). *Shewanella* can show resistance to imipenem by secreting oxacillinase.<sup>5</sup> At presentation, as the abscess was >5cms in dimensions, with necrosis of overlying skin, we

did incision and drainage in accordance with the recommendations for surgical management, Christian Medical College and Hospital, Vellore,<sup>6</sup> along with antibiotic coverage with colistin and breast emptying and regular dressing with Placentrex Gel.

## CONCLUSION

Even though *Shewanella* infection in humans is scarce, the number of reports has significantly increased over the last decade, suggesting that it indeed has a pathogenic potential. Though literature review suggests organism to be susceptible to beta lactamase antibiotics, the emergence of imipenem and beta lactamase resistant isolates is a concerning factor. As such, there is a need to look for such rare organisms and not to dispose all oxidase positive organisms as pseudomonas. It may not affect the overall outcome of the patient but will definitely help in better understanding of the epidemiology, pathogenesis and preventive aspects of such organisms.



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## CASE REPORT

# Endodontic management of type II dens invaginatus: a case report

Yaduka Pallavi<sup>1</sup>, Kataki Rubi<sup>2</sup>, Angami Neingutunuo<sup>3</sup>

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## ABSTRACT

*Dens Invaginatus is a rare developmental anomaly that occurs due to invagination of enamel organ. Due to its complex anatomy, it often leads to early involvement of the pulp. Its aberrant anatomy poses a challenge to the dentists in cleaning and shaping of the root canal and subsequent obturation. Knowledge of root canal morphology and its anomalies are important for the success of endodontic treatment. Advanced imaging techniques like Cone Beam Computed Tomography offer the advantage of detailed 3D imaging and are helpful in treatment planning compared to conventional radiographs. This article presents a case report on endodontic management of Type II Dens invaginatus.*

**Keywords:** Dens in dente, tooth anomalies, developmental anomalies, CBCT.

## INTRODUCTION

Complexities in root canal anatomy pose a challenge to the clinician in diagnosis and treatment. Dens invaginatus (DI), also known as Dens in dente, invaginated odontoma or dilated composite odontoma is a rare developmental anomaly resulting from deepening or invagination of the enamel organ into the dental papilla prior to calcification of the dental tissues.<sup>1</sup> It was first described as “a tooth within a tooth” by Salter in 1855 and was first described by Socrates in human tooth in 1856.<sup>2</sup>

The prevalence of Dens invaginatus ranges from 0.04 to 10%. The permanent dentition is more commonly affected than the deciduous dentition.<sup>3</sup> The teeth most affected are the maxillary lateral incisors (prevalence of 0.25–5.1%), frequently bilateral (43%), followed by central incisors, canines, premolars, and molars. Both maxillary and mandibular teeth are affected but mandibular occurrence of this anomaly is rare.<sup>4</sup>

Different classifications have been given by authors. The most common classification proposed by Oehler,<sup>5</sup> classifies DI into three categories according to the communication with periapical tissues and the depth of penetration. Type I is enamel-lined minor invagination occurring within the crown without extending beyond the cemento-enamel junction. Type II is enamel-lined invagination extending into the root beyond the cemento-enamel junction, remaining as a blind sac. Type III is invagination penetrating through the root to form an additional apical or lateral foramen.<sup>3,5</sup>

Dens Invaginatus is often missed during diagnosis and sometimes detected by chance on radiographs. The invagination is vulnerable to caries, which may lead to pulpal complications.<sup>6</sup> Once the pulp is involved, root canal treatment is required and is a challenge to the dentists. Therefore, early diagnosis is important so that the tooth can be restored before it progresses to infect the pulp.

This article presents a case of Type II DI with pulpal involvement where endodontic management was done.

## CASE REPORT

A 23 years old girl reported to the Department of Conservative

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### Address for correspondence:

<sup>1</sup>Post Graduate Trainee (**Corresponding author**)

**Mobile:** +919003153529

**Email:** pallavi.yaduka@gmail.com

<sup>2</sup>Professor

Department of Conservative Dentistry and Endodontics  
Regional Dental College, Guwahati.

**Mobile:** +919864010215

**Email:** rubikataki@gmail.com

<sup>3</sup>Post Graduate Trainee

Regional Dental College, Behind GMCH, Bhangagarh,  
Guwahati, Assam

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Dentistry and Endodontics with the chief complaint of pain in the right upper lateral incisor for the past 1 month. On clinical examination, the right maxillary permanent lateral incisor (12) was tender on percussion. There was discoloration in the developmental groove where the cusp blends with the sloping of the lingual tooth surface. The tooth showed no response to electric and thermal pulp testing. Past Medical history and dental history were insignificant. Intra oral periapical radiograph and Cone Beam Computed Tomography (CBCT) imaging were advised to the patient.

Radiographic report showed a radiopaque structure within the crown of 12, crossing the cemento-enamel junction and extending upto the middle third of the tooth. Widening of periodontal ligament was noticed (**Figure 1**). CBCT showed increased radiodensity similar to enamel within the canal wall in the palatal aspect due to the presence of type II DI which terminated in the middle third of the root canal (**Figure 2**). It revealed two pulpal areas, one central invaginated structure and a larger pulp space surrounding the central structure on all sides within the root canal (**Figure 3**). A single canal, approximately 5.4 mm going beyond the DI was seen.



**Figure 1** Pre-operative Radiograph



**Figure 2** Pre-operative CBCT Image



**Figure 3** CBCT image showing central anomalous structure surrounded by pulp

A diagnosis of chronic apical periodontitis was made based on the above findings. Root canal treatment followed by post endodontic restoration was planned. The clinical condition was explained and treatment consent was taken from the patient.

Local anaesthesia was administered. Rubber dam isolation and access opening was done. Working length determination was done using Apex locator (Root ZX, J Morita) and confirmed radiographically to be 20mm. (**Figure 4**).



**Figure 4** Working length determination radiographs

Complete removal of the central-anomalous structure was done to allow total removal of pulp tissue and create space for debridement and subsequent obturation of the root canal.<sup>1</sup> 25mm K-files were used to prepare the canals. Apical preparation was done till size 55. The canal was prepared by step back technique till size 80. Copious irrigation was done using 3% sodium hypochlorite, saline and 17% EDTA. The prepared canal was dried with absorbent paper points. Canal was obturated by vertical condensation using thermoplasticised gutta percha. Post endodontic restoration was done using composite resin. Tooth remained asymptomatic after a follow up of 3 months and 6 months (**Figure 5 and 6**).



**Figure 5** Post-operative radiograph



**Figure 6** Three months follow-up radiograph

## DISCUSSION

Several theories have been proposed to explain the etiology of dens invaginatus but it still remains controversial and unclear.<sup>6</sup>

In 1934, Kronfeld suggested that DI resulted from focal failure of growth of internal enamel epithelium while the surrounding normal epithelium continued to proliferate and engulf the static area.<sup>7</sup>

Rushton, in 1937, proposed that the invagination is a result of aggressive and rapid proliferation of a part of internal enamel epithelium invading the dental papilla.<sup>8</sup>

Atkinson, in 1943, suggested that DI resulted from external forces exerting an effect on the tooth germ during development.<sup>9</sup>

Oehlers (1957) suggested that distortion of the enamel organ during tooth development and subsequent protrusion of a part of the enamel organ leads to the formation of an enamel-lined channel ending at the cingulum or at the incisal tip.<sup>10,11</sup>

Genetic factors may play a role in formation of DI.<sup>12</sup>

Clinical presentation of DI varies considerably. Clinically, unusual crown morphology like dilated, peg-shaped, barrel-shaped teeth may be seen. The invagination allows entry of irritants into the area, which is separated from pulpal tissue by only a thin layer of enamel and dentine. This leads to development of dental caries which leads to pulpal involvement, sometimes even before root end closure. If untreated, it can lead to abscess formation, cysts, and internal resorption. There is high risk of perforation of the root canal walls when preparing access to the invagination.<sup>6</sup>

CBCT is essential for accurate diagnosis and treatment planning. They provide clear, detailed, 3D images in multiple slices, the number and location of canals, allowing a precise diagnosis of its type, extent, as well as the peri-radicular area.<sup>13</sup>

Complete debridement of the infected canal is the key to the success of endodontic treatment. Thermoplasticised gutta-percha can be useful for sealing anatomically complicated pulp spaces.<sup>14</sup>

## CONCLUSION

Lack of knowledge of anatomical variations and anomalies associated with each tooth and inadequate skills to manage them can lead to failure of endodontic treatment.

With the limitations of conventional radiographs, it is advisable to use newer diagnostic modalities like CBCT which are useful in the interpretation and treatment planning of complex teeth anomalies.

**Conflict of Interest:** None.

**Contribution of Authors:** We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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## REVIEW PAPER

# Analysis of the risk factors for sexual violence on women and its neurobiological aspects

Dutta DK<sup>1</sup>, Mahanta Putul<sup>2</sup>

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### ABSTRACT

*Sexual violence in the form of heinous offences like rapes, molestation, forced prostitution, female genital mutilations, paraphilias etc. has lately become a curse to the humanity by being one of the frequent and significant public health issue to both developed and developing countries. Being an insult to the civility, it is one of the leading causes of the severe and irreparable damage to the physical and mental health of the victims. With the development of the society the cases of sexual violence are going on increasing which is a big stigma to the mankind. Rape cases in the country have reported an increase of 12.4% from 34,651 cases in 2015 to 38,947 in 2016, the report has revealed according to the report released by National Crime Records Bureau (NCRB). Whereas according to National Family Health Survey (NFHS) an estimation of 99.1% of the sexual offences against women go unreported and these statistics shows the gravity of this curse to the society. But sadly till date nothing has been fruitfully done to prevent these offences. Interestingly extensive literatures have described that there are many factors which determine the etiologic profile of sexual violence in the society. Here in this paper the different risk factors which increases the predisposition of sexual offences is described which can be helpful in formulating the prevention strategies against the cause.*

**Keywords:** Rape; societal norms; hypersexuality; psychiatric disorders; monoamines.

### INTRODUCTION

According to WHO sexual violence is defined as: any sexual act, attempt to obtain a sexual act, unwanted sexual comments or advances, or acts to traffic, or otherwise directed, against a person's sexuality using coercion, by any person regardless of their relationship to the victim, in any setting, including but not limited to home and work. It includes a spectrum of acts including rape, molestation,

incest, child sexual abuse, harassment etc. India lies in the bottom five country when comes to the safety of women as stated in Gallup poll.

### Factors predisposing sexual violence

Risk factors for sexual assault are conditions, circumstances or characteristics associated with an individual or his or her environment that increase the likelihood of the individual becoming a perpetrator or a victim of sexual assault. The following risk factors are not the causes but their presence increases the risk for sexual assault.

### Factors involving men's risk of committing sexual offence

WHO have demonstrated individual factors, relationship factors, community factors & societal factors with correlation of men's propensity for sexual abuse.

### Individual and relationship factors

Alcohol and drug use, coercive sexual fantasies & other attitudes and beliefs supportive of sexual violence, impulsive and antisocial tendencies, preference for impersonal sex, hostility towards women, history of sexual abuse as a child & witnessed family violence as a child, family environment characterized by physical violence, strongly patriarchal relationship or family environment, emotionally unsupportive family environment & when family is honour considered more

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### Address for correspondence:

<sup>1</sup>MBBS Student, 5<sup>th</sup> Semester (**Corresponding author**)

Tezpur Medical College, Tezpur, Assam, India

**Mobile:** +919678850955

**Email:** diptakanthadutta@gmail.com

<sup>2</sup>Professor and Head

Department of Forensic Medicine

Assam Medical College and Hospital, Dibrugarh, Assam

**Mobile:** +919435017802

**Email:** drpmahanta@gmail.com

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important than the health and safety of the victim.<sup>1</sup>

### **Societal and community factors**

Societal norms supportive of sexual violence & of male superiority and sexual entitlement, weak laws and policies related to sexual violence, poverty, weak laws and policies related to gender equality & prevalence of high levels of crime and other forms of violence.<sup>1</sup>

Regarding psychological factors of offenders, such men often consider victims responsible for the rape and are not keen to know the consequences to the latter.<sup>3</sup> Victim blame was manipulated by varying the dress of the woman in the rape scenario (revealing or concealing) and the location of the rape (a library or a deserted park). On the other hand negative emotions such as disgust and guilt normally inhibit men from committing rape whereas macho attitudes adhering to a notion of masculinity that idealizes power, toughness, competitiveness, and aggression may indirectly disinhibit rape.

Moreover the constant association of pornography to sexual coercion is also evident. In a meta-analysis of 33 studies Allen et al. examined the association between pornography and nonsexual aggression by dividing sexually explicit material into three categories: (a) nudity, (b) nonviolent sexual behavior & (c) violent sexual behavior. Overall, results indicated an association between pornography and aggression. However, type of pornography was a moderator, such that exposure to nudity decreased aggression, whereas exposure to the latter two categories significantly increased aggression.<sup>4</sup>

A normal man is not aroused by a scene of sexual violence against a woman but certain circumstances like being angry at the women can alter that and can result to the arousals similar that of rapists. There was noticed a 50% decrease in blood flow by penile plethysmograph to the normal man's genital in response to scenes of rape or violence but it was not noticed in the case of the rape offenders instead their arousal was markedly stronger to the rape scene than to consenting sex.<sup>12</sup>

### **Factors related to women**

Though the victims are never responsible for the sexual violence against them but certain factors are seen to be constantly related which increases their vulnerability. Other factors influencing the risk of sexual violence include: being young, consuming alcohol or drugs, having previously been raped or sexually abused, having many sexual partners, involvement in sex work, becoming more educated and economically empowered at least where sexual violence perpetrated by an intimate partner is concerned & poverty.<sup>1</sup> Consuming alcohol or drugs makes it more difficult for women to protect themselves by interpreting and effectively acting on warning signs so can place them in higher risks for encountering offence. A study found that women who had experienced attempted or completed rape during childhood or adolescence were more likely to have a higher number of sexual partners in adulthood, compared with non-abused or moderately abused women, increasing their predisposition to rape.<sup>5</sup> Interestingly women with higher levels of education

is more likely to experience sexual violence than rest as found in a national survey in South Africa. It maybe because empowerment brings with it more resistance from women to patriarchal norms so that men apply violence in order to regain the control resulting in the offence.

### **Role of mental health**

The underlying causes of certain sexual offences are the altered state of mental health & can be associated with organic brain damage, disorders with congenital or acquired brain damage, head injuries (3.9%)<sup>6</sup> and abnormalities within the temporal horn as in sadist rapist.<sup>7</sup> It has been found that in certain psychiatric diseases like schizophrenia, there is a four fold chances of committing sexual offences and bipolar mood disorder especially in the maniac phase.<sup>8</sup> Other symptoms such as the increase of self-esteem, feelings of grandiosity, grandiosity delusions, considering oneself to be a special person, endowed with powers and high intelligence frequently present along with increase in the motor activity showing great physical vigour relating to the cause of offence.<sup>9</sup> Langstrom et al in their retrospective study on 535 rape offenders found the incidence of psychiatric background as the diagnoses were alcohol abuse or dependence (9.3%), drug abuse (3.9%), personality disorder (2.6%), and psychosis (1.7%)<sup>10</sup> According to DSM-IV sexual offenses against children are mainly by individuals with paraphilias like Exhibitionism, Pedophilia, and Voyeurism.<sup>11</sup>

### **Understanding the neuronal level in case of hypersexuality**

It is always very much important for understanding the neurobiology of the hypersexuality to know the causes of these violences. By hypersexual disorder, it encompasses sexual addiction and compulsive sexual behaviors involving the activation of neurotransmitters such as noradrenaline (NE) and oxytocin (OT), stimulating sexual arousal, and dopamine (DA) and melanocortins (MCs), stimulating attention and desire, within regions of the hypothalamus and limbic system, in response to sexual cues and stimulation. Their activation blunts the influence of inhibitory mechanisms, such as endogenous opioids, which are released in the cortex, limbic system, hypothalamus, and midbrain during an orgasm or sexual reward; endocannabinoids (ECBs), which mediate sedation; and serotonin (5-HT), which is released in those regions to induce refractoriness and sexual satiety. Sexual excitation can be primed internally by steroid hormone actions or externally by sexual incentives or drugs that activate excitatory neurochemical systems.<sup>2</sup> Any overexpression of these pathways can lead to hypersexuality like disorders.

In a recent survey with pedophilic patients, Mendez and Shapira demonstrated that brain disorders may trigger a predisposition to sexual attraction towards children through disinhibition and sexual preoccupation<sup>20</sup> as in cases of diseases of frontal lobe, striatum, temporo-limbic system and hypothalamus. Frontal lesions maybe accompanied by general disinhibition, including impulsive hypersexual symptoms; striatal lesions by increased in the triggering of sexual

response patterns and temporo-limbic lesions by disturbances in sexual appetite itself including the change in the sexual life.<sup>13</sup> Hypersexuality was found to be associated with subcortical disease in nonmotor basal ganglia, hypothalamus, or septal nuclei<sup>20</sup> and also in dementia, temporal lobe epilepsy and patients with frontal lobotomy.<sup>21</sup> Further ABC model (Stein, 2008) hypothesized the possible model for hypersexual behavior by stating that the Amygdala leads to affective dysregulation, Behavioral reward is controlled by the nucleus accumbens, where the concentration of the dopamine is seen to enhanced and ventral striatal circuits, and Cognitive control is impaired in the prefrontal cortex.<sup>14</sup>

### Endocrinology

The role of monoamines like serotonin (5-HT) and Dopamine(DA) has also been elicited in mediating the hypersexuality. 5-HT is involved in many psychiatric disorders, particularly mood disorder, and specifically depression, anxiety, schizophrenia, eating disorders, and obsessive compulsive disorder (OCD).<sup>16</sup> Stein et al have demonstrated the role of DA blocker and 5-HT reuptake inhibitor in controlling the hypersexual behavior. Increasing brain levels of 5-HT reduced sexual drive and sexual behavior and decrease showed opposite. Therefore drugs that increase 5-HT levels in the brain have been used to treat paraphilias.<sup>15</sup> Moreover Klos et al has been demonstrated that antiparkinsonism drugs which increases the DA level in the brain are related to hypersexual disorder,<sup>17</sup> which strengthens association the DA theory. Ristow et al(2018) has shown the reduced concentration of GABA in the dorsal anterior cingulate cortex in the cases of pedophilic offenders which demonstrates the role of GABA in treating hypersexuality.<sup>18</sup>

Some studies have stated that violent sex offenders have higher levels of androgens than nonviolent comparison groups correlating with sexual offences.<sup>22</sup> Thus testosterone has been shown to be related to the hypersexuality mainly the free testosterone, but few researches have also predicted that LH correlated significantly with sexual and violent recidivism<sup>19</sup> and thus the role of hypothalamo-pituitary-gonadal dysfunction also come into play. Meanwhile in a study with pedophilic men, Maes et al. found lower plasma Prolactin (PRL) levels in the pedophiles than in the controls.<sup>23</sup> PL has been seemed to play a negative feedback loop to modify the effects of the dopaminergic systems. The treatment of hypersexuality related disorders with SSSRIs, Antiandrogens & GnRH analogues is also noteworthy. SSRIs like fluoxetine increase serotonin levels by blocking the uptake of serotonin to its presynaptic neurons and increasing its concentration. Antiandrogens like cypoterone acetate (CPA) directly reduces the testosterone levels. GnRH analogue like Triptorelin decreases pituitary secretion of the gonadotrophins luteinising hormone (LH) and follicle stimulating hormone (FSH). This in turn inhibits the production of testosterone by the testes.

### CONCLUSION

Different literatures have shown that there are certain determinants reflecting the risk factors for sexual offences

and by eliminating these factors the incidence of such offences can be minimized manifold. Factors starting from the individual, societal to neuronal level; all can be to a certain level treated and prevented. Proper study must be encouraged regarding the detailed description of the underlying events regarding the etiology of sexual offences. Moreover by considering the above risk factors the urge of formulation of the preventive strategies for these offences must be promoted.

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## REVIEW PAPER

# Shaken baby syndrome- an unnoticed child abuse

Chakraborty Abhijay<sup>1</sup>, Sharma Rituja<sup>2</sup>

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### ABSTRACT

*Shaken baby syndrome or abusive head trauma is an injury to the baby's brain due to child abuse. It is known by different names such as Battered Child Syndrome and Abusive Head Trauma. It is an unnoticed crime. There is a law and clear guidelines in the developed countries such as USA, UK etc. But there is absence of law and specific guidelines regarding shaken baby syndrome in India. There is no way to detect this child abuse which is frequently taken place at the household as it is done by caretaker, parents themselves knowingly or unknowingly. This paper outlines about introduction of this specific type of child abuse, position in international perspective and Indian perspective with some judicial cases and suggesting of a necessity of proper law and guidelines in India regarding shaken baby syndrome.*

**Keywords:** *Infant abuse; international perspective; Indian perspective.*

### INTRODUCTION

Shaken baby syndrome or Abusive Head Trauma is injury to the baby's brain due to child abuse. Cause of this injury is due to direct blows to the head, dropping or throwing a child or shaking a child. Shaken baby syndrome is known by different names such as Battered Child Syndrome and Abusive Head Trauma. It has been called as a silent child abuse as the victim is not able to complain about its problem. In the past physical abuse has been taken out of picture, but the recent studies depict that there is infant abuse under 1 year of age is head trauma.<sup>1</sup> It has been observed that Shaken baby syndrome is the leading cause of death in child abuse cases in the United States. The reason for this is the anatomy of the infants which puts them in the higher risk in particular action. It is tragic that the parents don't intend to harm the infant but because of their fragile constitution, even a brief shaking may result into the irreversible injury and even death.<sup>2</sup> The beaten child syndrome was described by Ambrose

Tardieu in 1860, but shaken baby syndrome (SBS) is clearly described in the medical literature only a century later by Caffey in 1972.<sup>3</sup> He formulated the term "whiplash shaken baby syndrome", based on 27 cases of child abuse with hematoma injuries. Caffey first noticed non-accidental injury of childhood or child abuse syndrome in 1946, who reported multiple fractures of long bones in six infants suffering from chronic subdural hematoma. The long bone fractures appeared to be traumatic origin, but, the traumatic episode and actual causative factors or mechanism remained obscure.<sup>4</sup> It was remained unnoticed until early 1960 when Henry Kempe and his colleagues give a new terminology "Battered Child Syndrome".<sup>5</sup> In shaken baby syndrome what happens is when the infant is grabbed around the torso and shaken, or by grabbing of their limbs and swinging them. The shaking motion typically occurs for 5 and 20 seconds results in quieting the baby- the most common intended effect. The perpetrators, however, does not realize that the infant has stopped crying not because he was soothed but by brain damage occurred. In many states of USA, abuse is defined as the infliction of injury on a child by parent or guardian. Abuse is differentiated from neglect, which usually refers to failure of parents or caretaker to provide the child with adequate physical care and supervision. Abandonment of child also means neglect.

### Shaken Baby Syndrome Diagnosis

Sometimes and often situation occurs where shaken baby syndrome is alleged, the history of shaking is not diagnosed, in reality, there may be complete absence of any history of

### Address for correspondence:

<sup>1</sup>Research Scholar, PhD (Law) (**Corresponding Author**)

**Mobile:** +917490972139, +919411178263

**Email:** abhijay.chakraborty@gmail.com

<sup>2</sup>Associate Professor

Faculty of Legal Studies, Banasthali Vidyapeeth, Rajasthan

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trauma or otherwise very slight trauma which is not associated with the symptoms experienced by the victim. In some cases parents and caretakers admit the shaking of the baby. If we study the medical literature, most texts referring to diagnostic triad for diagnosing shaken baby syndrome requires the following triad of injuries: Subdural Haemorrhage (SDH), Encephalopathy and Retinal Haemorrhage (RH).

The traditional conception is that these injuries are the result of serious injuries or trauma such as motor vehicle accident or fall from a multi-storey buildings or violent shaking. However, this opinion is currently being challenged by evidence to the contrary.

### **Shaken Baby Syndrome in International Perspective**

Shaken Baby syndrome is growing concern across the world. In United States, shaken baby syndrome gained notoriety during the period mid 1990s as a result of Louise Woodward trial. The Supreme Court of United States held that the Due Process clause of the Fourteenth amendments provides parents a fundamental right to custody of their children, stating "a natural parent's desire for and right to the companionship, care, custody and management of his or her children is an interest far more precious than any property right". It is to be noted that this right is not absolute as government holds *parens patriae* in protecting citizen. *Parens patriae* is a doctrine by which a government has standing to prosecute a lawsuit on behalf of a citizen, especially on behalf of someone who is under a legal disability to prosecute the suit.<sup>6</sup> But after Dr. Kempe's Classification of Shaken Baby Syndrome in 1962, gave great heed to child abuse. He had also proposed the child abuse cases should be reported by the practitioners. In France, the study shows 30000 children are abused each year and 400 children die. Most unlikely and unlike the most other criminal matters, once SBS is diagnosed the burden of proof effectively shifts to the parents or to the caregiver to disapprove a medical diagnosis- classic *res ipsa loquitur*.<sup>7</sup> The news article titled "tough time for Jaipur couple as US slaps 'shaken baby syndrome' on infants" was distributed featuring that couple from Jaipur is confronting extreme time in America as the administration forced Shaken Baby Syndrome (SBS) when their youngster allegedly unintentionally fell on the floor and got head damage. Since the administration forced SBS on the infant, the biological guardians lost his authority and he has been given over to temporary parents.<sup>8</sup> In New York, According to the study of New York Department of Health, there are estimated 1000-3000 infants shaken every year. One in four shaken infants will die, and 80% of those that don't die suffer permanent injury.<sup>9</sup> In Romania, no statistical data exists as the shaken baby syndrome is not recognised. United Nations Conventions on the rights of the child declares basic rights and standards for the maltreatment. In United States of America if any paediatricians have suspicion as to the maltreatment of the infant, it is his mandatory duty to report the such incident to the local child welfare agency. In some countries like Belgium and Holland the cases of maltreatment are dealt with

confidentially through health and social workers. In North Carolina cases of shaken baby syndrome is dealt with efficiently. In Virginia, the study was made and it was estimated that during 2003-2007, the perpetrator in 54% of the cases were parent or guardian, it also states that period between 2003 and 2007, there were 26 deaths which are classified as Shaken Baby Syndrome. Of these 26 deaths, 4 were shaken as infants and died later as complications resulting from their injuries, there were older than 2 years of age and died of shaken baby syndrome. The crude 5 year death rate for all deaths during this duration was 0.35 per 100000 children younger than 15 years of age. It is alarming situation in Virginia. In South Africa, though there is no reported case law is available but now there is expansion of awareness of shaken baby syndrome. It must be noted that medical practitioners who on reasonable grounds believe that a child was abused or there is maltreatment of child, and in the event they report in such a bona fide belief are protected from civil liability in terms of sections 110(3) of Children's Act 38 of 2005. Australian remedy for the shaken baby syndrome was simple- prosecution was based solely on the presence of one or more triad symptom would not be sufficient to prove a case of criminal abuse beyond a reasonable doubt on the absence of corroborating evidence. Australian interrogation was done on the basis of criminal appeal and has undergone a huge change in investigation and prosecution of alleged Shaken Baby Syndrome. In Australia through the judgment of Supreme Court in various cases, there is a development of law on Shaken Baby Syndrome. Though it was not a solution for past cases, Australia's integration of the conservation on, and growing of shaken baby syndrome in 2003 was a solution to preserve the integrity of shaken baby syndrome cases prosecuted in years to come.

### **Shaken Baby Syndrome in Indian perspective**

According to the United Conventions on the rights of the children in which India also ratified in the year 1992 all children are born with fundamental rights which are right to survival to health, life, nutrition, name, nationality. Right to Development to education, care, leisure, recreation, cultural activities. Right to Protection from abuse, neglect, and exploitation. Even though India's one-third population is of children, there's interest have never been given priority and these rights have been violated every day. If we see the constitution of India, Fundamental Rights under Part III has been guaranteed to the people of India. Under Part IV of the Constitution of India, Directive Principles of State Policy in Article 45 it is provided that "The state shall endeavour to provide early childhood care and education for all children until they complete the age of six years".<sup>10</sup> In India, child abuse is rampant, According to National Crime Record Bureau, In percentage terms, major crime heads under 'Crime Against Children' during 2016 were kidnapping & abduction (52.3%) and cases under the Protection of Children from Sexual Offences Act, 2012 (34.4%) including child rape.<sup>11</sup> These figures suggest that there is crime committed against children in other offences but there is no case of shaken

baby syndrome as it shows that there is no legal provision regarding shaken baby syndrome, no mechanism to track shaken baby syndrome. There is a need to think about a legislation regarding shaken baby syndrome as it exists in developed countries. Though cases of non-accidental head injuries are reported in India but lack of awareness about shaken baby syndrome it remains unnoticed. Literature search shows only few cases. There is a lack of data regarding the extent of child battering that takes place within households or institutions. As already stated there is no way to know how many cases of shaken baby syndrome has been reported in India. Over a decade, there are only few cases which were reported in some journals in India. What a pity, when there is a case of shaken baby syndrome and when such child is discharged from the hospital and to go back to the same household where they suffered abuse, at times they suffered even death.<sup>12</sup>

## CONCLUSION

Shaken Baby Syndrome is a very controversial topic in medico-legal practice and it is evident from the discussion highlighted above that there is requirement of the law relating to shaken baby syndrome. Child abuse hampers the basic values of humanity. The time has come that both our medical and legal system should take immediate step to prevent this child abuse in the form of shaken baby. It is also evident that there is a law and guidelines about shaken baby syndrome in developed countries. India is land of villages and there may be many cases of shaken baby syndrome which remains unnoticed. Even medical practitioners working in villages have lack of knowledge about shaken baby syndrome so they can't detect them. India is a land of superstitions also. As there is no awareness about shaken baby syndrome, cases of abuse is dealt under the guise of superstitions. As already stated that time has come not only the medical and nursing practitioners should be aware but also the members of the legal field such as lawyers, investigating agencies, and the court should be enlightened about the child abuse. The policy makers in the legislature should also develop some laws relating to Shaken Baby Syndrome.

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